

Innovative Techniques in Cardiac Surgery Using the Apex of the Heart

PhD Thesis

Imre Kassai MD

Semmelweis University
Doctoral School for Clinical Science in Medicine



Consultant: Péter Andréka MD, PhD

Reviewers: Zoltán Galajda MD, PhD
László Gellér MD, PhD

PhD Final Examination Board Chair: Mátyás Keltai MD, PhD, DSc
PhD Final Examination Board: Andrea Szűcs MD, PhD
Viktor Molnár DVM, PhD

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The principal investigator of the studies evaluating the most valuable innovative methods described by this thesis is

Tamás Szili-Török MD, PhD.

The international part of these studies is running under his supervision, in the Department of Clinical Cardiac Electrophysiology, Thoraxcentre, Erasmus MC, Rotterdam, The Netherlands

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List of Abbreviations

ACBG	– aorto-coronary bypass graft
AO	– aorta
AV	– atrio-ventricular
Bi-VAD	– biventricular assist device
BTR	– bridge to recovery
BTT	– bridge to transplant
CABG	– coronary artery bypass graft
CAD	– coronary artery disease
CK	– creatine kinase enzyme
CK-MB	– creatine kinase myocardial isoenzyme
CPB	– cardiopulmonary bypass
CRT	– cardiac resynchronization therapy
CS	– coronary sinus
DCM	– dilated cardiomyopathy
ECG	– electro-cardiogram
FDA	– food and drug administration
ICD	– implantable cardioverter-defibrillator
ITA	– internal thoracic artery
HTX	– heart transplantation
LAD	– left anterior descending coronary artery
LPA	– left pulmonary artery
LV	– left ventricular
LVAD	– left ventricular assist device
MCS	– mechanical circulatory support
MIDCAB	– minimally invasive direct coronary artery bypass
NYHA	– New York Heart Association
OPCAB	– off-pump coronary artery bypass
OM	– coronary artery obtuse marginal branch

PCI	– percutaneous coronary intervention
PVAD	– paracorporeal ventricular assist device
PUBL	– own publication
RA	– right atrium
RCA	– right coronary artery
RPA	– right pulmonary artery
RV	– right ventricle
TA-CRT	– transapical cardiac resynchronization therapy
trI	– cardiac troponin I
trT	– cardiac troponin T
TEE	– transesophageal echocardiography
VAD	– ventricular assist device
VSD	– ventricular septal defect

1.

Introduction

The relationship between the apex of the heart and cardiac surgery is controversial. There are only a few entities of surgically curable diseases of the heart that directly involve the apex itself. The apex, however, should still be considered a significant part of the heart.

Historically there were two major obstacles on the way of surgeons to treat heart diseases. On one hand manipulation involving the internal structures while the heart has to maintain the circulation and on the other hand the avoidance of the deteriorating effect of artificial circulatory support were problematic for decades. The apex was one of the first regions of the heart that gave hand to the surgeons to solve these problems. Thousands of patients suffering from rheumatic mitral stenosis were treated successfully with closed commissurotomy, when the most appropriate instrument, the Tubbs dilator was positioned in the mitral orifice by insertion into the left ventricle through the apex of the heart. This was also wide-spread method in Hungary in the 1960s and 1970s. It provided treatment option for larger group of patients, because the higher cost of operations with heart-lung machine reduced significantly the number of valve surgeries applying the open procedure. Surgeons at my work, at the time, the Hungarian Institute of Cardiology, kept this method in practice still in the late 1980s, therefore I had a unique opportunity to take part in these operations before the last Tubbs dilator took its well-deserved place in the museum.

But not exclusively the pioneers' work was efficiently supported by opportunities of the cardiac apex. Innovative techniques using the apex have been continuously developing in every field of cardiac surgery as described in the following chapters.

1.1 - The role of the left ventricular apex in better myocardial preservation during cardiac operations

Small things can cause big changes... also in cardiac surgery and also at the very beginning. As mentioned in the introduction, a revolutionary new era of cardiac surgery started, when CPB made the intracardiac repairs possible. Surgery provided better survival in most end-stage cardiac disease than medicinal treatment. Careful patient selection, however, was necessary, because cardiac operation involving CPB caused high early morbidity and mortality rate in those years. CPB maintained the appropriate circulation and oxygenated blood supply for the body and vital organs, but the heart could be easily damaged during aortic cross clamp regardless of the different myocardial preservation techniques (PUBL. 1). After series of autopsies it was consequently observed that in the vast majority of postcardiotomy deaths the most damaged part of the myocardium was the subendocardium. The reason of this subendocardial injury was easily hidden underneath the ice-slash cover during delivering cardioplegic solution. After CPB started and the heart arrested or ventricular fibrillation developed the ventricular cavity tended to dilate. The intracavitary and subendocardial pressures elevated, and the perfusion of the subendocardial myocardium stopped. It was impossible to provide blood or cardioplegic solution supply into that area, and the too long and mostly warm ischemic period destroyed a great mass of subendocardial myocardium. The consequences were untreatable. After a perfect CPB an excellent intracardiac repair the heart could not recover regardless of the longer and longer reperfusion periods. The only remedy of this terrible problem was to prevent the ventricular dilation after starting the CPB and stopping the regular and effective contractions of the ventricles. Surgeons had to apply suction to decompress the left ventricle, otherwise the outcome was immeasurable. There are a lot of possibilities to place the vent-cannula: pulmonary vein, pulmonary artery, right atrium-atrial septum, right ventricle outflow tract, aortic root, and the apex. They provide different suction effect and need different management during suction and after decannulation. The opening of the left side of the heart for insertion of the cannula is also important in

terms of timing, intracavitary pressure and forward ejection. Without careful planning air embolization may occur.

The most successful, therefore the safest and most cost effective localization for inserting a left ventricular decompression cannula is **the apex**. It was even more important in the early era of open heart surgery, when special cannulas were not available, and intraoperative monitoring devices (e.g. TEE) for detecting left ventricular dilation, were not in use either.

1.2 - Aortic valve disease – alternative treatment options using the apex of the heart

Despite the clear indications for aortic valve surgery a relatively large patient population with otherwise surgically treatable severe aortic disease is not suitable for the operation because the risks of the standard valve surgery are too high in their condition. There are several ways to reduce these increased risks with careful preoperative patient management. Some alternative surgical techniques for various stages of the standard operation are also helpful. For example the partial median sternotomy leaves a great part of the sterno-costal joints intact therefore provides better chest stability and respiratory function after surgery. Furthermore, there are two revolutionary new methods with more significant risk reduction. The apex of the heart is involved deeply in both of them.

1.2.1 Aortic valve bypass

Implantation of a valved conduit between the apex of the left ventricle and the aorta is curative when severe aortic stenosis is presented without significant aortic valve insufficiency. It can be performed through thoracotomy without aortic cross-clamp. Due to this possibility patients with severe co-morbidities, including “porcelain ascending aorta” can be treated with relatively low operative risk.

1.2.2 - Transapical aortic valve implantation

This technique is a modality of a method that originates from a completely different idea formulated in the field of valve disease treatment. This is a catheter-based intervention to eliminate aortic valve dysfunction, both stenosis and insufficiency. An effective valve structure is modified in its geometry to achieve cigar-form with capability to transport it from the outside of the body into the aortic orifice, and in that position its geometry is restituted with only catheter manipulation. When the transport is difficult through the arteries and the aorta, the apex of the left ventricle is the feasible solution. For this purpose two devices are already used clinical practice: CoreValve[®] and the Edwards Sapien[®] equipped with transapical implantation kits. For this type of implantation a mini-thoracotomy is sufficient above the apex of the heart.

2.

Aims

Our aims were to evaluate the leading role of the apex in the revolutionary innovations of cardiac surgery in the recent years.

1. Assessment of the role of the apex in Off Pump Coronary Artery Bypass (OPCAB) operations.
2. Safe connection is necessary between the heart-lung machine and the main arteries of the body for surgical treatment of acute proximal aortic dissection. The establishment of the safe connection is impeded by the dissection itself. We evaluated the role of apical cannulation in establishing cardiopulmonary bypass in regard to the perfusion of vital organs.
3. Surgical treatment of heart failure with long term mechanical circulatory support providing whole body perfusion is one of the recent revolutionary techniques. Our aim was to apply this method in Hungary too. To achieve our goal we also evaluated the role of apical cannula implantation in safe and effective long term mechanical circulatory support.
4. Another increasingly important treatment of the heart failure is the Cardiac Resynchronization Therapy (CRT). We developed a fundamentally new approach for alternative LV lead implantation for CRT. Our prominent aim was to evaluate the effect of our new method in the ratio of responders to CRT.

3.

Methods

1. After the initial experience with OPCAB operations (1995), we “re-engineered” our team work in the theatre (1999) and performed this type of operation for isolated coronary artery bypass in all relevant cases. We examined the feasibility of the method with performing elective recoronarography in the first 27 consecutive patients. We conducted an extended study to evaluate the early and mid-term results in the first 209 patients operated after September 1999. We compared the results with patient groups that were operated with heart-lung machine on the basis of indication of non-elective postoperative recoronarography. These control groups were set up from patients of two different cardiac surgery centers of Hungary. We conducted further studies to evaluate the role of apical suction device in hemodynamically better heart positioning for OPCAB. We evaluated its effect in patients with severe multivessel coronary artery disease. We compared the results achieved when for surgical treatment at least one over 9 mm length distal anastomosis was necessary with results when only regular length distals were necessary. Our other study was the comparison between the blood levels of CK, CK-MB and cardiac troponins after coronary bypass operations without and with heart-lung machine in 315 and 196 patients, respectively after 2003.
2. We studied the possible causes of malperfusion in vital organs during operations to treat acute proximal aortic dissection. We evaluated the risks of unattended connection between the heart-lung machine and the main arteries of the body during artificial perfusion. The native and artificial perfusions in acute proximal aortic dissection are only identical when the arterial cannula inserted through the apex in the left ventricle and led through the aortic valve into the proximal

ascending aorta. We also evaluated the efficacy of this type of cannulation in our clinical practice.

3. We studied the long term mechanical circulatory support to treat heart failure and the possibilities to perform this treatment in Hungary too. Long term mechanical circulatory support has two significant risks of complications. One is a device related infection; the other is a thromboembolic/hemorrhaging complication. We evaluated these possible complications in relation with apical cannula implantation. We assessed the role of long term mechanical circulatory support in pediatric heart transplantation with regard to donor heart shortages and progression behavior of heart failure in childhood.

4. After we developed a fundamentally new method for CRT (2007), we evaluated the feasibility of our method by collecting data during and after the first 10 operation. We assessed the risks of other alternatives of CRT and other possibilities for endocardial pacing of the left ventricular lateral wall in comparison with our method. We compared the results achieved with surgical epicardial lead implantations and the results with our transapical endocardial lead implantations in 12 and 10 patients respectively. Heart failure patients with some type of congenital heart diseases and some type of surgical corrections of their congenital heart disease are not suitable for standard CRT with coronary sinus lead implantation. We assessed the characteristic features of this patient group and the exceptional possibility for CRT of these patients with our method.

4.

Results, discussion

4.1

Off-pump coronary bypass operations: key position for positioning the heart

Myocardial preservation is one of the most important issue to reduce invasiveness of cardiac operations, as described in Chapter 1.1. On the other hand, myocardial preservation is more problematic when the coronary arteries are diseased, and the distribution of the cardioplegic solution is not equal in different parts of the myocardium. In these cases the preserving effect during the aortic cross clamp time is missing where the heart is not cold enough and not at minimal oxygen consumption level in diastolic arrest. It is more quite evident, that if the operation can be performed without global ischaemia of the myocardium, it has to be an advantage over those techniques where aortic cross clamp is used. Moreover, the direct coronary revascularization can also be performed without using CPB. This possibility is the other operative risk reducing factor in off-pump coronary revascularization.

The key to this method is the adequate positioning of the heart, which allows performing anastomosis on any surface of the heart without reducing the capability to maintain the adequate circulation. The techniques of heart positioning were changed before the most appropriate method, application of the **apical suction device** has been developed.

The innovation was encouraged by the excellent results of OPCAB operations with less sophisticated instruments and/or only one or two target surfaces of the heart with less

positioning. My personal experiences with OPCAB procedures started in that era (PUBL. 2). I had the opportunity to study the results of the operations that I performed using this technique with my colleagues in my work at that time: Zala County Hospital (PUBL. 3). Firstly, we examined the feasibility of the method with performing elective recoronarography in the first 27 consecutive patients. The results were excellent and I started to perform the operations in all consecutive patients suffering from isolated CAD from January 2000 (PUBL. 4). Secondly, we performed an extended study to evaluate the early and mid-term results in that patient group, and to compare the results with patient groups that were operated with CPB on the basis of indication of non-elective postoperative recoronarography (PUBL. 5). These control groups were collected from patients of two different cardiac surgery centers of Hungary: Zala County Hospital and Gottsegen György Hungarian Institute of Cardiology. The most important details of this study can be summarized as follows:

4.1.1 - Short- and midterm follow-up of off-pump coronary artery bypass patients

Our early results with consecutively used OPCAB have been demonstrated earlier. In this study we analyze why OPCAB is more cost-effective than other myocardial revascularizations according to our short- and midterm follow-up data. 209 patients were included in the study group. One surgeon operated them between September 1999 and August 2001. In 1999 the OPCAB ratio was increased step-by-step and by January 2000 all coronary artery bypass operations were performed without CPB in isolated CAD. In these 209 consecutive patients the average number of distal anastomoses was 3.07. 208 patients who had been discharged after the operation were examined in our outpatient clinic 30 and 60 days after surgery. We ensured that patients were examined by their own cardiologists. We interviewed our patients via phone or mail in August and September 2001. If it was necessary we performed further examinations. For comparison we took into consideration the early recoronarographies after on-pump coronary artery bypass in two Hungarian centers in the study period. There was no angina or myocardial ischaemia at the examinations in the second postoperative month

in the off-pump group. We had data available of 194 patients (93.3%) by the end of the study period. The follow-up periods varied between 1-23 month (an average of 12.42 months). 3 late deaths occurred (1.4%), one of them was certainly non-cardiac related. Acute myocardial infarction did not occur in the rest of the patients during the study period. Recoronarography was not necessary in the study group. The control data showed 4.3 and 4.6% of on-pump patients who needed recoronarography. We analyzed the results of recoronarographies in our center. 3 were negative and 13 were positive (3.7% of on-pump patients). In all positive cases the patient had a significantly narrowed or occluded graft. 2.6% of on-pump cases needed re-revascularization (3 percutaneous and 6 operative procedures). Our OPCAB cases showed excellent results. We were able to reduce the operative stress and resource utilization without any loss of graft quality. Early graft patency results are directly related to surgical technique, therefore we would say that OPCAB is the most cost-effective method for the revascularization of our patients today.

Our earlier studies on consecutively used OPCAB operations are extended in this study on short- and midterm follow-up results.

In a short period revolutionary changes took place in cardiac surgery. A lot of new operative procedures appeared. We perform so extensive interventions in human organism, that have never seen before. Cardiac surgeons operate in every age-bracket of patients, even performing major operations. This evolution is impeded by two obstacles. On one hand there are some contraindications in cases with certain co-morbidities, even with some physiological disorders. On the other hand there is the higher cost due to high-tech equipments and increased ratio of complications after major surgeries. All methods that can successfully overcome with these obstacles are welcome in our field. Our data reveal that OPCAB is one of these methods.

In many respects OPCAB is not definitely new. The first efforts on myocardial revascularization (1) such as some early coronary endarterectomy and the in situ

applications of ITA as their rescue solution (2), as well as the sporadic planned bypass operations in the early 1960s (3) were all performed without CPB.

A lot of cardiac operations could have been done after CPB had appeared (4). Owing to the good influence of CPB, Favarolo's method (5), the Aorto-Coronary saphenous vein Bypass Graft (ACBG) operation spread rapidly. Early, basic studies – Veterans Administration (VA) Randomized Trial, European Coronary Surgery Study, Coronary Artery Surgery Study (CASS) – showed the balance between effectiveness and indication of ACBG operations. This operation was more beneficial than medicinal therapy only in patients who suffered from significant left main stem stenosis or significant three-vessel disease with at least one proximal significant stenosis of a great branch. The reasons of this outcome were the patency rate of the saphenous vein grafts and the risk of the operation. Better outcomes could have been achieved even in the early postoperative results of ACBG if complete revascularization had been done. The main reason was the global myocardial ischaemia during the preparation time of the distal anastomoses. The global myocardial ischaemia and the additional deteriorating effect of CPB caused myocardial stunning and low ejection fraction in the postoperative period. The medicinal treatment against these circumstances created a very serious situation in every non-revascularized myocardial territory. Acute myocardial infarction, rhythm disturbances, further loss of left ventricle function, low cardiac output syndrome and untreatable “circulus vitiosus” were not rare complications in cases without basic treatment of ischaemia. Researchers realized soon that primarily global myocardial ischaemic injury should be prevented. Probably most cardiac surgery studies have revolved around myocardial protection since Bretschneider's early publications (6) (PUBL. 1). For the same reasons the operative risks were significantly higher in patients with severe CAD without at least one antegrade filled, significantly narrowed, graftable great branch. The extra work put forth during the operations to achieve complete revascularization could be beneficial in the long run too. On one hand the functional importance of the angiographic stenosis could have been less precisely assessed at that time. Surgeons could not be sure if one graft was more important than another. With more grafts there was better chance to survive until collaterals developed and some of the vein grafts finally occluded.

Significant difference was observed in long-term patency rate between saphenous vein grafts and ITA grafts. The results were better with ITA grafts (7). For this reason the ITA was used more and more in coronary surgery. These interventions were called Coronary Artery Bypass Graft (CABG) operations rather than ACBG, because the naturally formed central end of the in situ ITA graft is not in direct contact with the aorta.

In addition to global myocardial ischaemia, the other main obstacles of ACBG, CABG operations were the less favorable effects of CPB (8). CPB technique was continuously and thoroughly changing to reduce its hazards, and this important work has not been finished with success yet.

Managing their well-known limitations, on-pump CABG operations can be performed successfully when the classic indications are presented. It is important to compare their outcomes with the results of new methods.

The first re-discovery of the off-pump technique was in South America. Its cost-effectiveness played an important role in that. Successful long-term results in big series were reported by Buffolo (9) and Benetti (10) in 1990 and 1991. A few unsuccessful results were also reported at that time. Some new stenosis developed near the anastomoses in the early postoperative period (11). The reasons of these unsuccessful results were the wrong technique of local coronary artery occlusion to provide bloodless field for performing anastomoses, and the absolutely bad practice of immobilizing the heart with snares around target coronary arteries. These problems were easily eliminated later, but the fact is that OPCAB was unfairly neglected for years.

After those years the second “Renaissance” of OPCAB has started partly due to external influence. The less and minimally invasive techniques have spread rapidly in medicine and especially in other surgical fields. The PCI played an increasing role in treatment of CAD patients. The procedure caused stress with PCI is significantly less than with CABG. But late outcomes after PCI are less successful than those after surgical revascularization. The required way of evolution has been clearly seen: to keep quality of surgical revascularization, but to reduce intervention caused stress. The internationally well-known pioneer of this technique, Calafiore reported his early results in 1996 (12). The Minimally Invasive Direct Coronary Artery Bypass (MIDCAB) can reduce operative stress, because CPB is avoided and it only needs a small incision. This

operative approach can be mostly useful when only one area of the heart needs intervention.

Results of MIDCAB operations showed that reproducible, precise construction of anastomoses is possible on the beating heart. The MIDCABS's advanced mechanical stabilizer devices can be used in the regular operative approach too. So we can revascularize surgically without CPB patients with three-vessel disease nowadays.

As far as I know the first OPCAB operation in Hungary was published by the author of this thesis in 1994 (PUBL. 2).

We assess the short- and midterm follow-up data of consecutively used OPCAB method. As demonstrated earlier there were less operative stress and reduced initial resource utilization, so we had excellent early results, but we examined if our results could promise better cost/benefit ratio in the long run too. The most important comparative study: Bypass Angioplasty Revascularization Investigation (*BARI*) and other studies with mainly similar target (*EAST, RITA, CABRI, GABI, ERACI*) presented the results of Percutaneous Transluminal Coronary Angioplasty (PTCA) in patients who could have been treated with this method too. The results of these studies were partly superseded by new PCI techniques which can reduce the restenosis ratio. We presume there is a benevolent competition between cardiologists and cardiac surgeons. Considering the interests of patients, can surgeons gain an advantage with OPCAB and MIDCAB techniques?

Our study can answer this question by the following reasons:

- presently used PCI techniques can not provide as good patency rates as can be reached after surgical revascularization
- the prices of the instruments used in PCI techniques increase cost
- early graft patency results are strongly related with the technique itself, which means if a method do not decrease patency rates at short- and mid-term, it will unlikely decrease them in the long run when the outcomes are rather determined by the natural history of the disease
- our patient selection and operative technique could reduce limitations of the study

- our technique for OPCAB reduced cost in every case.

In September 1999 we decided to increase the ratio of OPCAB in our coronary surgery practice step-by-step. The gradual way was necessary, because the OPCAB technique does not only demand alternative surgical approach, but also requires a new type of cooperation in the theater. The most important thing is the close contact between the operating surgeon and the anesthesiologist. By January 2000 our team could perform off-pump procedures safely and successfully in all CAD patients (Figure 1). This fact had been verified by elective recoronarography studies of 27 patients. We demonstrated these excellent results in the congress of Hungarian Society of Cardiology in May 2000 (PUBL. 3).

Performing or not performing OPCAB is always an intraoperative decision. As the most experienced surgeon of our center I did not set any operative technique related limitation to perform OPCAB. There was no other restrictive co-morbidity in this patient group besides combined operations. Circulatory conditions of the patients could have been normalized without CPB in acute cases. So I could perform OPCAB in all consecutive, isolated CAD patients after January 2000. We operated one-vessel diseased patients if they were not suitable for PCI, and two- or three-vessel diseased patients in our center. We did not do any operative method related selection when we distributed patients among surgeons. So we thought our study of these patients was an appropriate method to receive an accurate answer to our question.

Figure 1 shows the monthly number of the 209 patients who were operated for isolated CAD between September 1999 and August 2001.

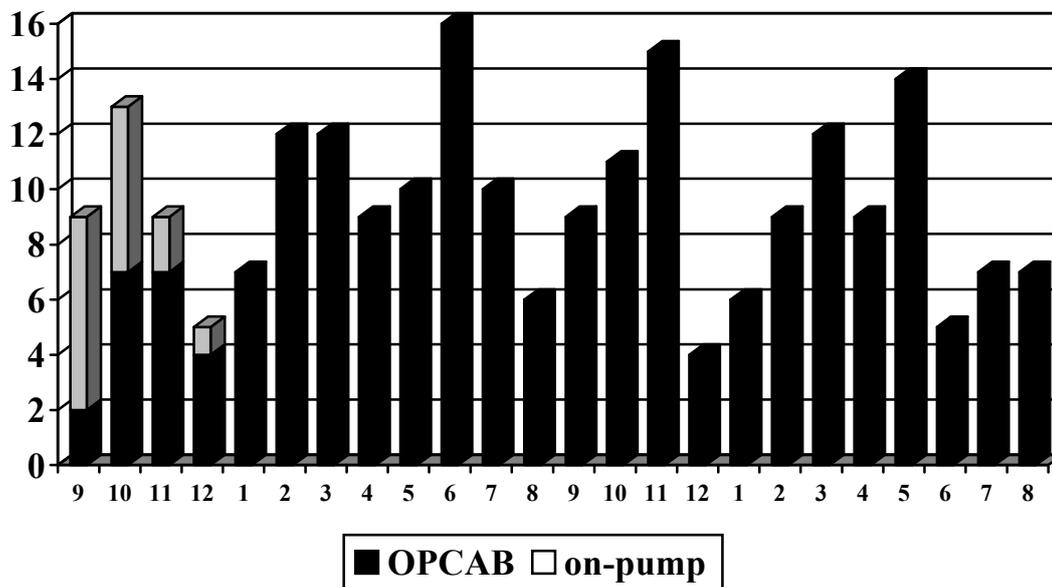


Figure 1: monthly number of the 209 OPCAB patients

Baseline clinical characteristics in the study group did not show significant differences from any other CAD patient group (Table 1).

Table 1: clinical characteristics of patients in the study group

	min – max	Average
Age	35 – 89	60.34 years
	number	%
Male	127	61
Previous AMI	167	80
Diabetes	61	29
Hypertension	123	62
Hypercholesterolemia	107	51
Impaired LVF (EF<40%)	44	21
Significant left main stenosis	46	22
Unstable angina presents at operation	38	18
Previous atrial rhythm disturbances	16	8
Previous PCI	59	28
Previous CABG	38	18

Figure 2 shows the age distribution of patients. 37 patients (17.7%) were older than 70 years at the time of the operation.

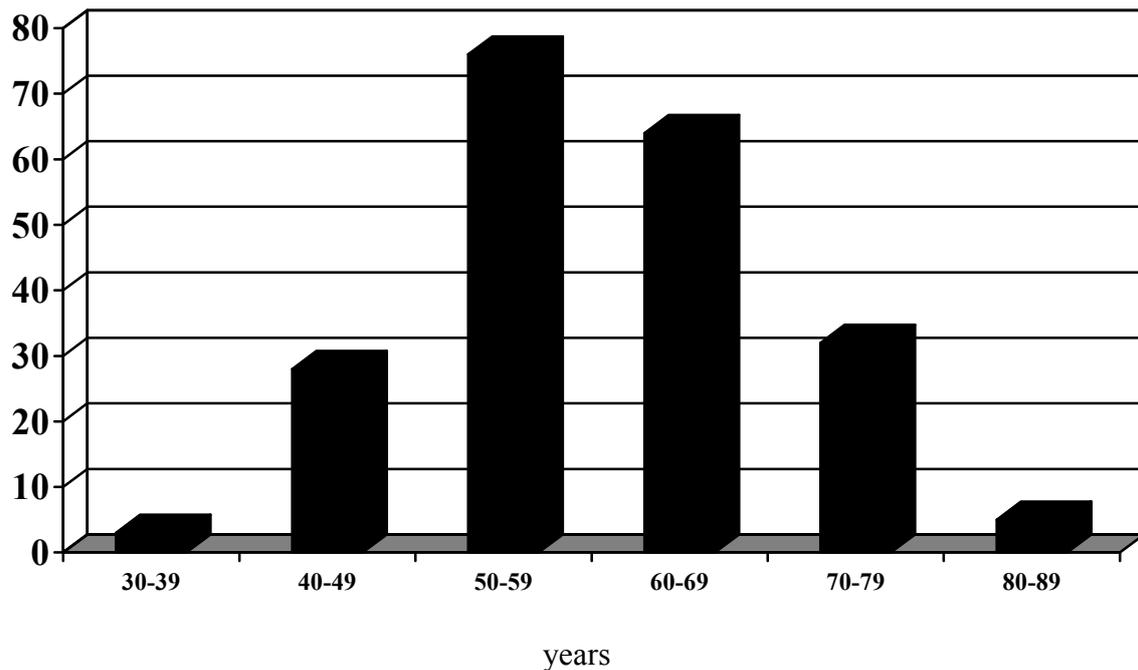


Figure 2: age distribution of patients (n)

84 patients (40.2%) were included in the high-risk group according to their severe CAD or co-morbidities or by reason of their age.

We had little experience with “hybrid” revascularization. There were only three “hybrid” procedures. In one of them the PCI part of revascularization failed, in another case early restenosis developed after PCI. Therefore we excluded these two patients. We kept one patient who was planned for “hybrid” intervention. However, the PCI part was not done, because the angiography at the time of the planned PCI did not re-justify significant stenosis in the target vessel.

Distal anastomoses were performed at the territories of all three main vessels from the beginning of the study. In 1999 the number of the distal ends ranged from 1 to 5, the average was 2.54. After January 2000, in the 190 consecutive patients the number of the bottom ends ranged from 1 to 8, the average was 3.07.

Only 4 patients did not receive ITA graft (98.1% of the patients grafted with at least one ITA). Both ITAs were used in 12% of the operations. The proximal parts of the used ITAs were always fully mounted. Their distal parts were mobilized as long as it was necessary to reach the target area in some cases on the fully enucleated heart. We always used ITAs with their surrounding tissues. Papaverin has always been injected in these tissues carefully. In some cases when ITAs and saphenous veins were not acceptable in quality or length we used radial arteries.

We always started the procedures with the identification of the target points of the diseased coronaries. The heart-lung machine and the disposable parts of the CPB circuit were in a medium level stand by. We carried all equipments into the operating room, but we did not unpack them.

We did not use Cell-saver. After opening the chest, ITA was mobilized and before dividing it heparin was given in 1 ml/body-weight dosage. We gave a higher dose of heparin if intra- or aorto-coronary shunts were used. Heparin supplementation was based on regular activated clotting time controls. We only used bone wax in the presence of excessive marrow bleeding after chest opening, and the wax was always eliminated at the end of the operations. Remaining effect of heparin was always neutralized at the end of the surgery.

No myocardial preconditioning was applied. We prevented myocardial ischaemia. The most important strategy to prevent ischaemia was to make a plan for the sequence of anastomoses. Important conditions were the original anatomy of coronary arteries (dimensions, supplied myocardial mass), the locations and degree of flow reduction, the existing collaterals and retrograde filling. If one approach (mainly of circumflex territory) was significantly unfavorable for the beating heart than the others, it was always the last. We performed 5 (2.4%) left anterior thoracotomy when only postero-infero-lateral branches needed grafts. Via median sternotomy first the LAD or proximal

RCA territories were grafted. We began with the largest occluded artery or with occluded artery with better retrograde filling. If there was no occluded artery on these two territories we began with sequential graft on arteries with multiple lesions. In these cases the first anastomosis was performed side to side on the smaller branch and if it was a vein graft or a free arterial one the central anastomosis was immediately the second. The last step was the end to side anastomosis on the bigger vessel. If there were no arteries either with multiple lesions or with diseased side branches we used shunts (in only 8%).

We used different exposures for different territories:

Wet gauze in the pericardial sack	LAD
Deep pericardial retraction sutures	LAD, intermediate
Right atrial – acute margin retraction suture	proximal RCA
Enucleation with slings, which were run through the transvers sinus and under inferior vena cava, or which were anchored in the oblique sinus	all, except proximal RCA

We utilized Trendelenburg position to maintain haemodynamic stability.

If it was necessary we used a simple pressure action stabilizer that was fully reusable.

The bloodless field for the anastomoses was achieved with 4/0 Prolene snares and teflon pledgets. The arteries were carefully pressed with them avoiding any injury.

Figure 3 and 4 show the intraoperative situations in different exposures for different territories.

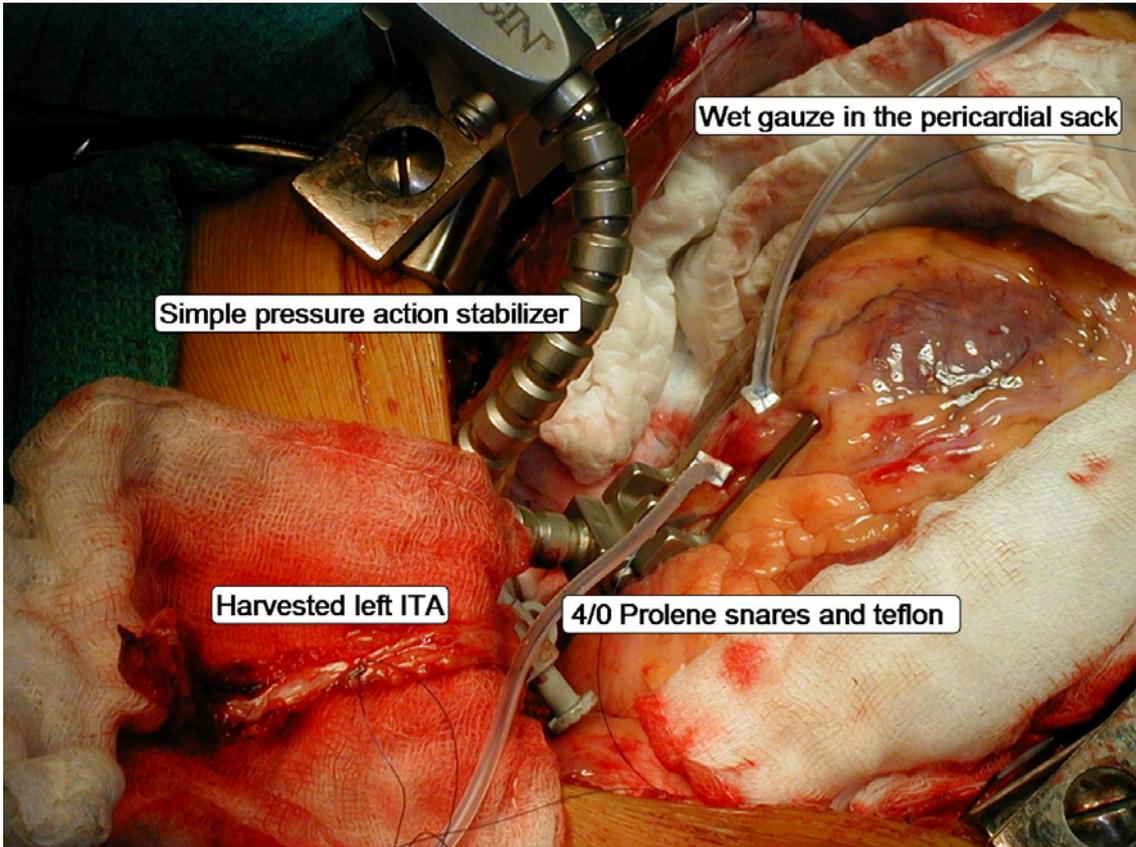


Figure 3/A

Exposure for grafting the LAD territory with sequential left ITA conduit: initial step to perform left ITA to diagonal branch side-to-side anastomosis

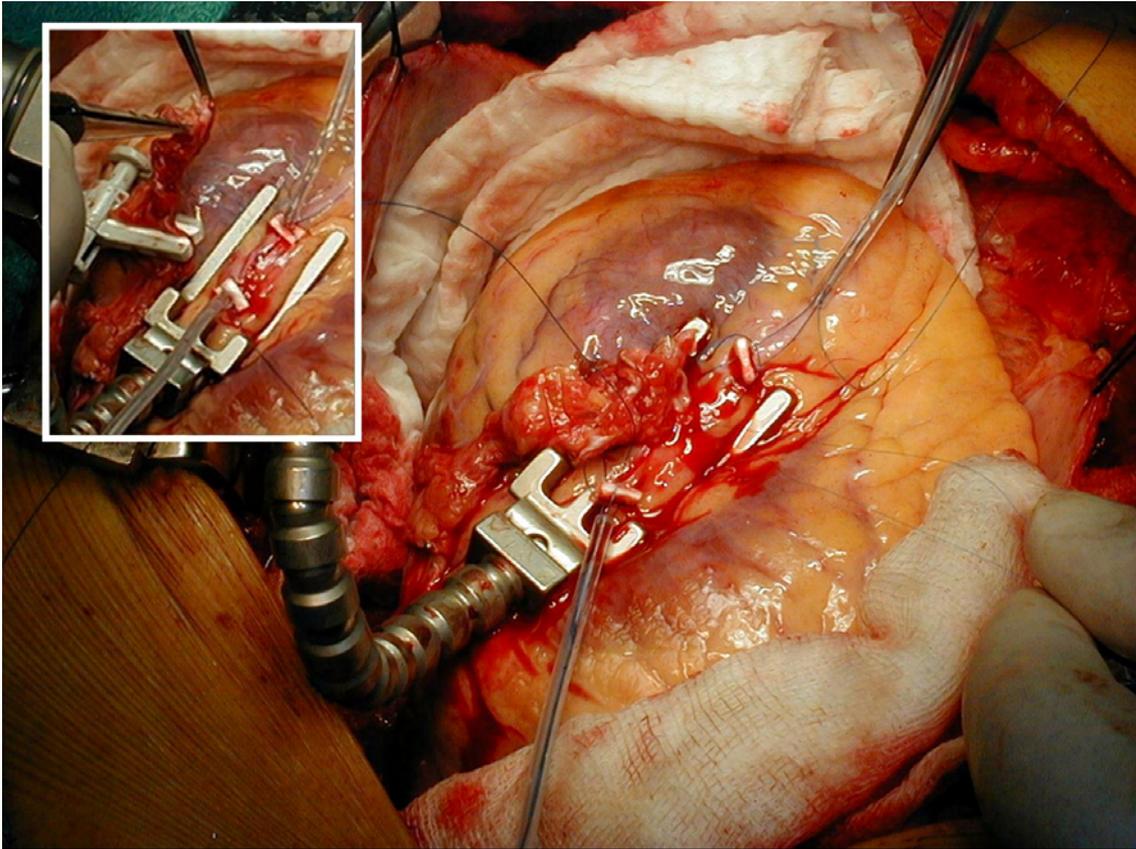


Figure 3/B

Further steps of performing left ITA to LAD end-to-side anastomosis

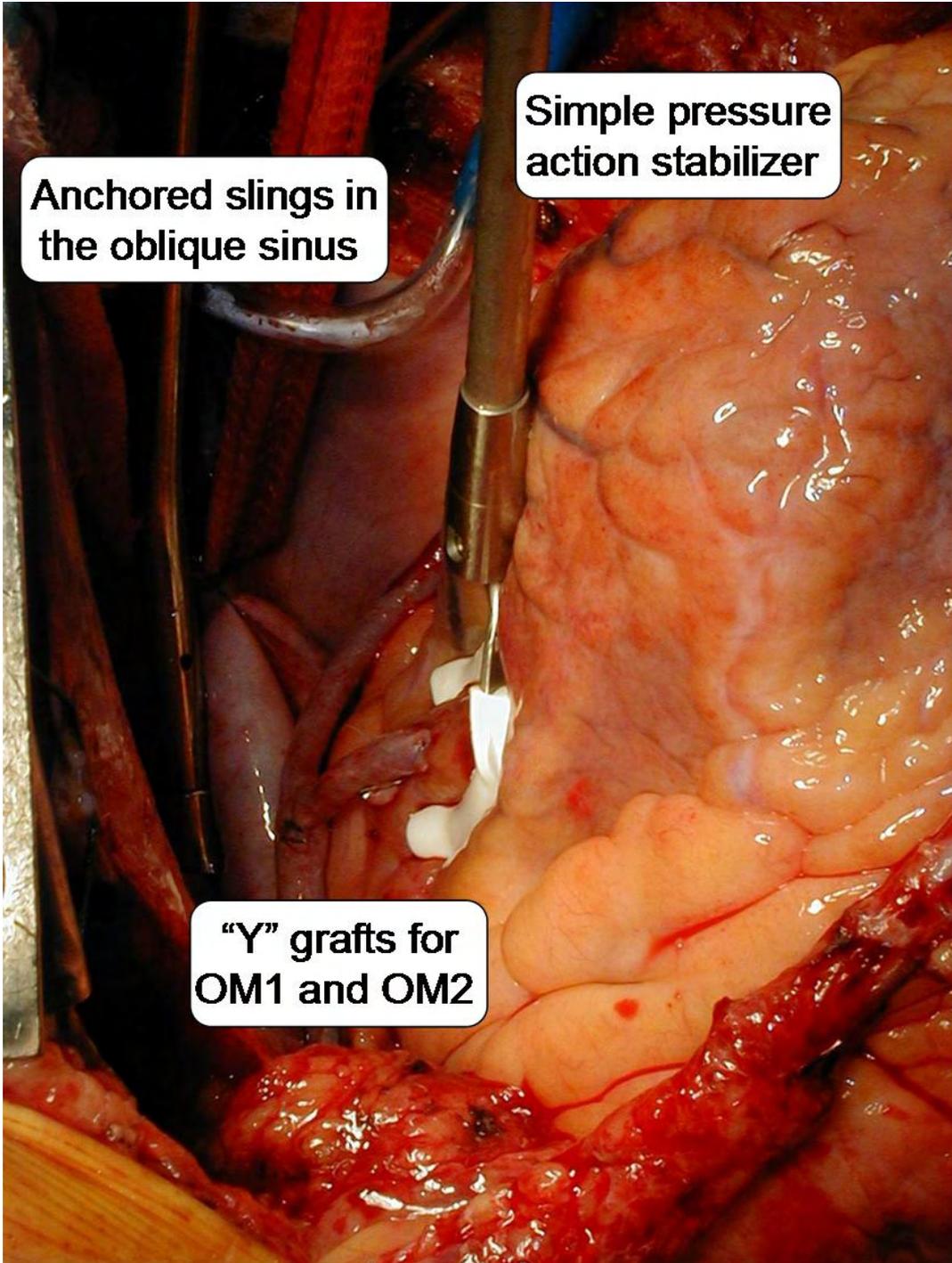


Figure 4

Exposure for grafting the circumflex territory

The anastomoses were made regularly with 7/0 or rarely 6/0 or 8/0 Prolene running suture. We frequently formed sequential grafts with two or sometimes three distals and “Y” grafts with two, three, four or in exceptional cases five distal ends. Due to these types of grafting we could reduce the number of manipulations on the aorta.

The closing ceremony and the postoperative management were similar to our on-pump cases.

There was one operative death (0.4%). This patient died early in the morning on the first postoperative day due to ventricular fibrillation a few hours after extubation in good clinical conditions. His resuscitation was unsuccessful. Autopsy did not find any myocardial injury, the grafts were patent.

There was one myocardial infarction (new Q waves) (0.4%), without any circulatory consequence.

There were 2 new atrial fibrillations (0.9%) and 5 malignant ventricular rhythm disturbances (2.4%) during the operations. All of them were electrically treated immediately.

There was no need for conversion for any reason during the operations.

There was one operative complication that needed intervention (0.4%). After protamine administration we just closed the patient when right ventricle expansion and airway pressure increasing were detected, AV block, malignant ventricular rhythm disturbances appeared, and the circulation collapsed. Possibility of massive pulmonary embolism was arisen. We established CPB and asked for TEE to find out the reason. Before having the TEE result, we observed flow reduction in the RCA graft. We pulled down the bottom end, but the field was clear and high-pressure flow was detected through the graft from the aorta. There was only one difference: the previously presented distal back-flow disappeared. We extended the coronarotomy and to our great surprise we found a mostly white thrombus in the bifurcation of the RCA. This thrombus could have been peeled off easily. After the removal no intimal injury was visible in the coronary artery. The anastomosis was re-sutured. The TEE finding was also surprising. There was a ribbon like thrombus in the left atrial appendage. We could bind the appendage from the outside. The TEE justified that there was no any residual thrombus in the left side of the heart. The CPB was weaned easily and the recovery was uneventful.

There was another ventricular fibrillation and circulatory collapse in another patient. She was in the bathroom when she collapsed on the 4th postoperative day. Her resuscitation was successful and the acute recoronarography confirmed that all grafts were patent. The further postoperative period was uneventful.

There was no major neurological event. Minor events occurred in 3 patients (1.4%). There was no postoperative renal insufficiency. 3 patients (1.4%) had transient respiratory problems, but none of them required ventilation more than 24 hours. There was no massive gastrointestinal bleeding, and only 4 patients mentioned slight abdominal discomfort (1.9%). There was one deep sternal wound infection (0.4%), which was successfully treated with antibiotics and with closed antiseptic irrigation-drainage system. Superficial wound problems were treated locally in 5 patients (2.4%).

208 patients who were discharged after operation were examined in our outpatient clinic between 30 and 60 days after surgery. We ensured that patients were received by their own cardiologists. We interviewed our patients via phone or mail in August and September 2001. If there was any need we performed further examinations.

For comparison we counted the early recoronarographies after on-pump coronary artery bypass surgeries in two Hungarian centers in the study period. One was our center and the other was the second largest in Hungary according to the annual operation number. The latter was my former and recent workplace. I worked there until August 1999 and returned in January 2007. All of our patients were examined in one of these two centers before their operations. That is, the study group and the control group were collected from the same patient population.

We also analyzed the results of recoronarographies in our center and counted the necessary re-revascularizations.

We were able to examine all the 208 discharged patients in the second postoperative month. Each patient was free from chest pain. Early treadmill tests were performed in 146 patients (70.2%). No angina or silent ischaemia were detected at these tests. 162 patients (77.9%) had already been reviewed by their own cardiologists before their

examination at our outpatient clinic. The importance of the personal contact with the own cardiologist was emphasized again for all patients.

None of them was presented due to complaint or symptoms caused by myocardial ischaemia in the follow-up period.

Two patients had pain related to the sternal wound. The problematic sternal wires were removed. In two other cases we excised painful keloids.

The follow-up time was 1-23, on average 12.42 months. The follow up was executed in 194 patients (93.3%). There were 3 late deaths (1.4%), among these there was one certainly non-cardiac death. Acute myocardial infarction did not occur in the rest of the patients in the study period. There were 15 hospitalizations (7.2%) due to other complaints, symptoms or co-morbidities. Other surgery was done in 10 patients (6.7%). 185 patients (95.3%) got into better stadium after the operations. There was also no need for recoronarography in the study group.

In the second largest Hungarian center called Gottsegen György Hungarian Institute of Cardiology 1275 patients were operated for isolated CAD with CPB in the study period. There were 55 (4.3%) recoronarographies. The duration between operations and recoronarographies ranged from 1 day to 20 months the average was 3.5 months. 44 recoronarographies followed the operations within one year. In the Zala County Hospital 347 patients were operated for isolated CAD with CPB in the study period. There were 16 (4.6%) recoronarographies. The duration between operations and recoronarographies ranged from 1 to 18 months the average was 8.7 months. 11 recoronarographies followed the operations within one year.

In these two centers 1622 patients were operated all together for isolated CAD with CPB in the study period. There were 71 (4.4%) recoronarographies. The average duration between operations and recoronarographies was 4.7 months. 55 recoronarographies followed the operations within one year (33.9%).

We analyzed the results of recoronarographies in our center. 3 were negative and 13 were positive (3.7% of on-pump patients). There was no patient without significantly narrowed or occluded graft in the positive studies. 2.6% of on-pump cases needed revascularization (3 percutan and 6 operative procedures). 10 positive studies followed the operations within one year.

Our OPCAB cases showed excellent results, in accordance with some other studies (13, 14, 15, 16, 17, 18). These authors published 98.8, 95, 96, 98.9, 95 and 95.6 % patency rates of all grafts, respectively in follow-up periods ranged from 2 days to 36 months. According to these data the graft patency in off-pump cases is at least equivalent to graft patency in on-pump CABG. Our early graft patency was 100 % at the 27 elective recoronarography.

Compared the recoronarography rates after operations in our study the results of OPCAB are at least equivalent again to results of on-pump cases (table 2).

Table 2: results

	OPCAB	GOKI CPB	ZMK CPB
Average follow-up duration (month)	12,42	3,5	8,7
Rates of postoperative recoronarography (%)	0	4,3	4,6
Rates of positive studies (%)	0	n.a.	3,7
Rates of studies within one year (%)	0	3,5	3,1
Rates of re-revascularizations (%)	0	n.a.	2,6

GOKI: Gottsegen György Hungarian Institute of Cardiology

ZMK: Zala County Hospital

n.a.: electively not collected data

Numerous studies justified cost reduction due to OPCAB (19, 20, 21, 22, 23, 24, 25).

We were also able to reduce costs of patients care as a result of the following factors:

- the heart-lung machine and the disposable elements of the CPB circuit were in a medium level stand by, so they could have been used in another operation without limitation
- we did not apply disposable stabilizers

- we used only a low number of shunts, because we prevented myocardial ischaemia by careful planning of the sequence of the anastomoses rather than using shunts in every vessel
- we were able to reduce the complication rate also in the high-risk group due to less operative stress

This benefit was in addition to reproducible, precise creation of anastomoses on the beating heart.

According to our results we would say that OPCAB is the most cost-effective method today for revascularization in two- and three-vessel CAD and in patients with one-vessel disease who are not suitable for PCI.

4.1.2 - Studies with the most sophisticated positioning systems: the apical suction devices

As a result of the changes in the financial possibilities which allowed the use of advanced positioning devices, for example the Medtronic Starfish[®] and Octopus[®], the OPCAB caught on rapidly. More and more surgeons became familiar with the method, some of them, as the leaders of their unit, followed the famous Belgian coronary surgeon, Paul Sergeant, and “re-engineered” their coronary surgery practice, switching from the on-pump to the off-pump technique. Unfortunately some important details are still missing in a number of centers. In others, the individual OPCAB surgeons are still not supported by anesthetists who prefer the on-pump technique; in other words, the systematic “re-engineering”, which involves the whole team, has not taken place at these places.

The most important element of this re-built coronary surgery is the appropriate mobilization of the heart with an apical suction device, for example the Medtronic Starfish[®] (Figure 5).

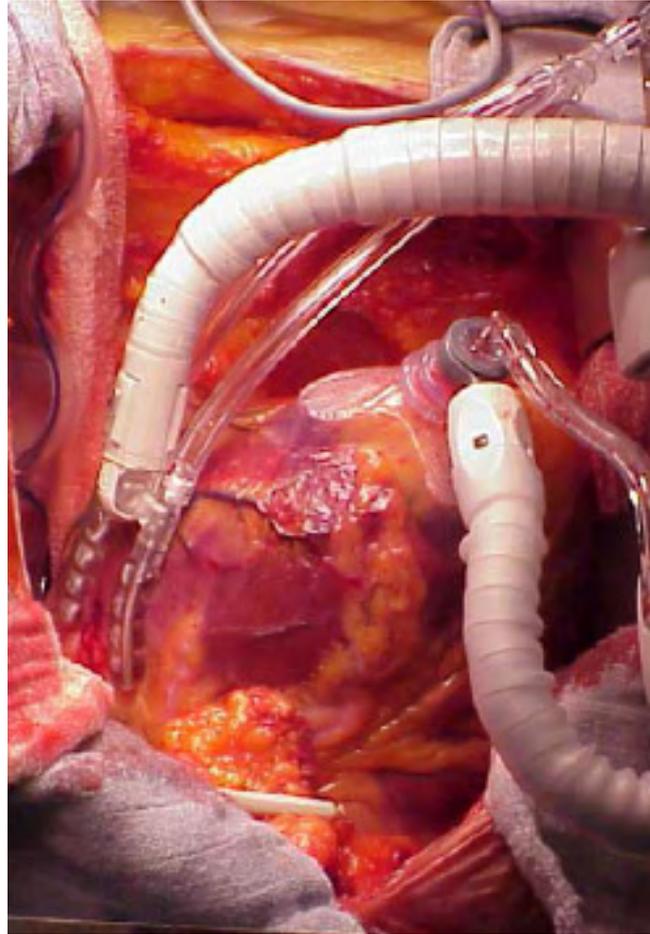


Figure 5

The Medtronic Starfish[®] and Octopus[®] “working together”

The advantages using this type of devices were evident in my own practice, too. It was absolutely necessary, because the main features of CAD also changed in patients referred for surgery. The percentage of patients previously treated by PCI increased significantly and we found more and more coronary arteries with severe atherosclerotic diseases on their distal part. I studied these new challenges in OPCAB surgery in 2002 (PUBL. 6).

Since the correlation between the complexity and length of distal anastomoses is more definite in cases of OPCAB, patients were collected with at least one bottom end over 8

mms in length. Figure 6 shows the intraoperative finding and solution of distally diseased coronary artery.

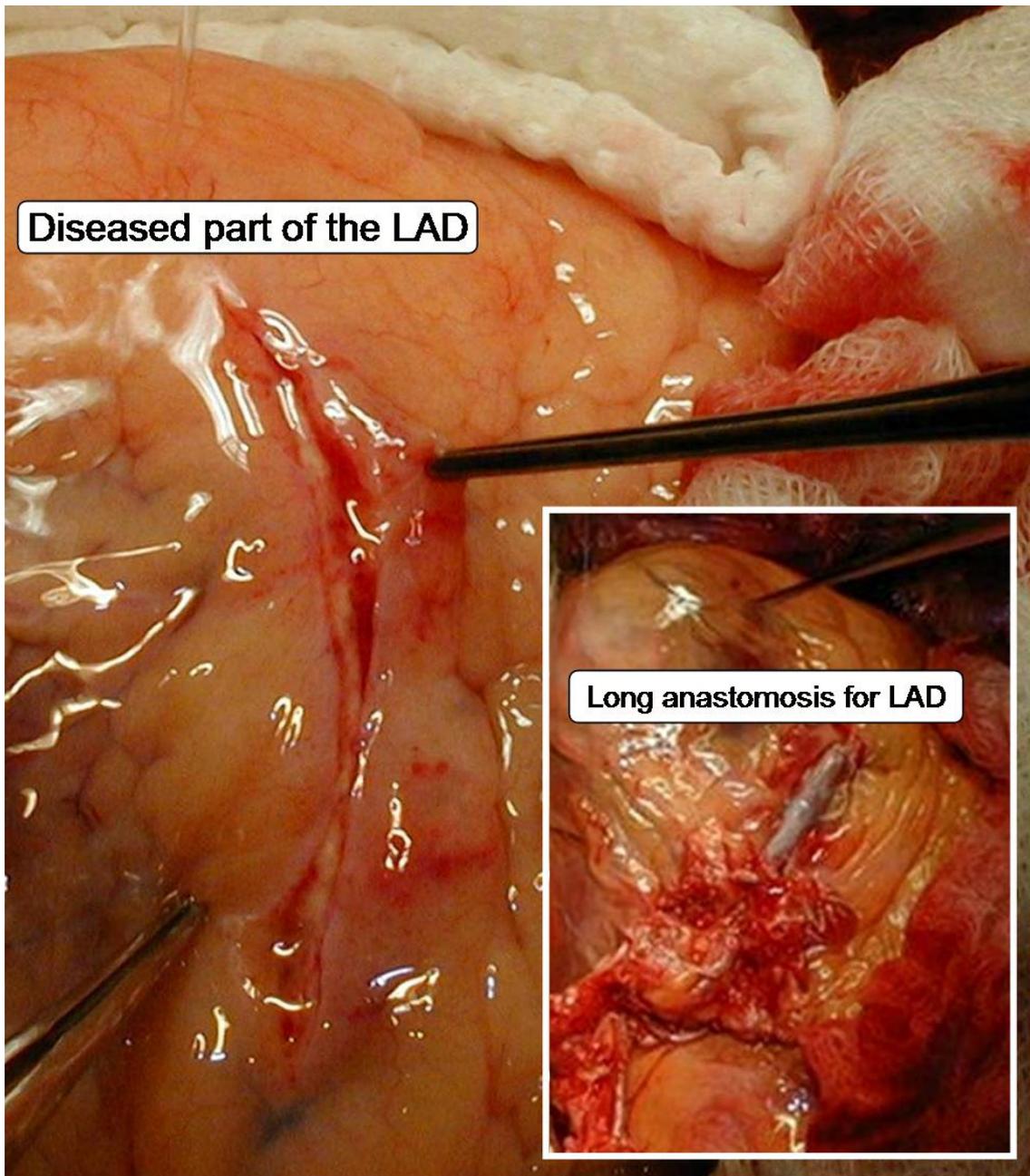


Figure 6

Diffuse atherosclerosis of LAD with several significant stenosis. The solution was a sequential left ITA to LAD/LAD grafting with a long distal LAD anastomosis using the left ITA-end extended with saphenous vein patch on the distal part of the 30 mms long distal LAD coronarotomy.

Operation-related enzyme release and follow-up data were compared among patients with and without long distal anastomoses. 93 long distal anastomoses (14.7 % of all distal ends) were found in 67 patients (32.05 % of all patients):

(mm)	9	10	12	14	15	16	17	18	20	22	24	26	27	28	30
(pc)	5	13	24	18	6	7	1	4	1	5	3	1	3	1	1

The postoperative blood levels of CK-MB (U/l) were slightly lower after performing long distal ends:

	min	max	average
at least one distal \geq 9 mms	7	114	28,26
distals only < 9 mms	7	203	30,15

The only patient who suffered perioperative myocardial infarction proved by pathologic ECG changes was also in the group of shorter distal anastomoses. There was no significant difference between the functional classification of patients with and without long distals at the end of the follow-up period:

	NYHA I	NYHA II	NYHA III
at least one distal \geq 9 mms	75 %	20 %	5 %
distals only < 9 mms	77 %	19 %	4 %

According to this study there was a general tendency to refer patients for surgical revascularization with more and more distally diseased coronary arteries. The OPCAB method was an appropriate solution for revascularization in these challenging anatomies, also using the advantages of aforementioned sophisticated positioning devices.

I had another opportunity to study the modern OPCAB technique after 2003 (PUBL. 7), when the possibility to measure the serum cardiac troponin levels became available in all patients (PUBL. 8).

There were 315 patients in the study group (OPCAB) and 196 patients in the control group (CPB-CABG) operated between 1 January 2003 and 31 May 2004. There was no significant difference in the EuroScore levels of these groups, 2.91 ± 2.27 vs. 3.22 ± 2.35 ($p=0.158$).

Blood samples were collected at the end of the operations (sample-1), on the first postoperative day (sample-2) and – to analyze the serum CK and CK-MB levels – very often on the second postoperative day (sample-3). According to the available troponin kits in the laboratory we measured troponin I (trI) or troponin T (trT) in the different periods during the study.

We evaluated the collected data with ANOVA GLM statistical method in SPSS software. The panels of Figure 7 show the results.

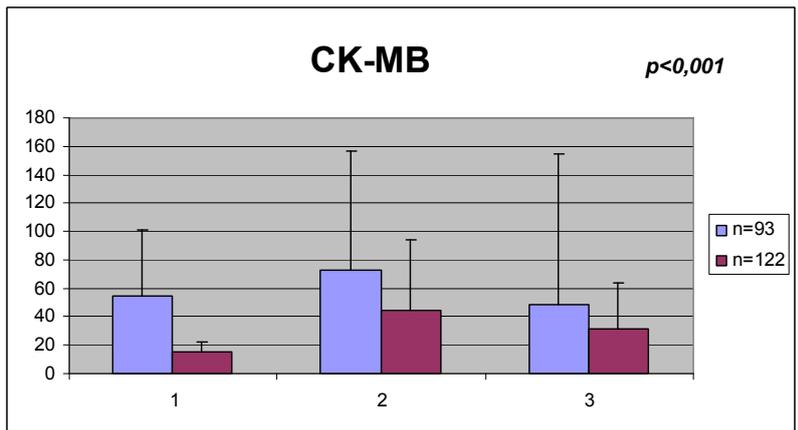
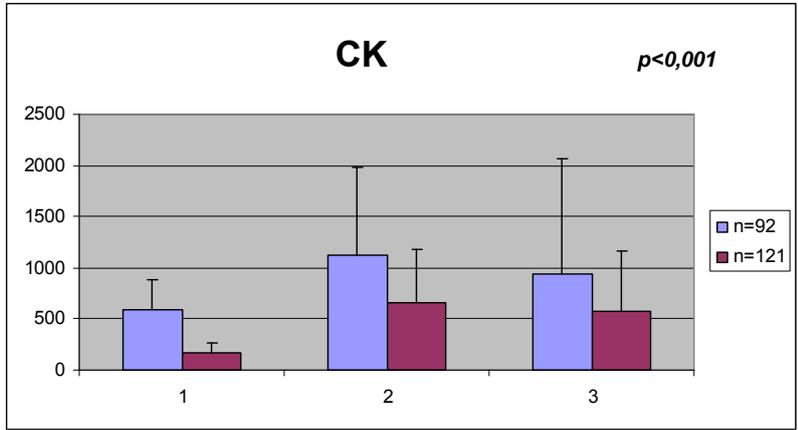
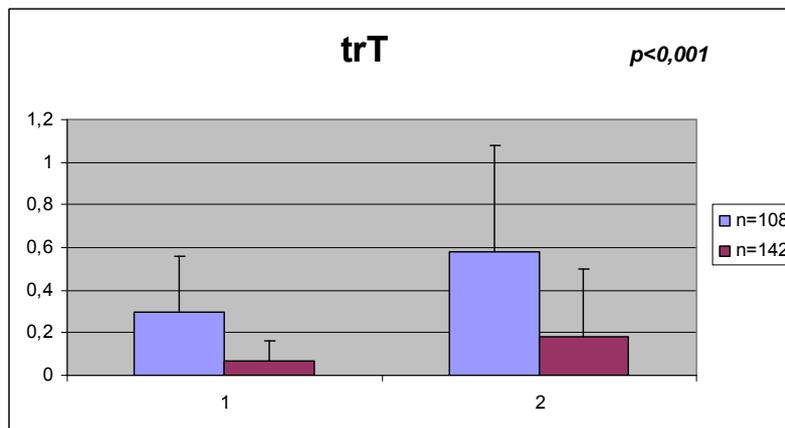
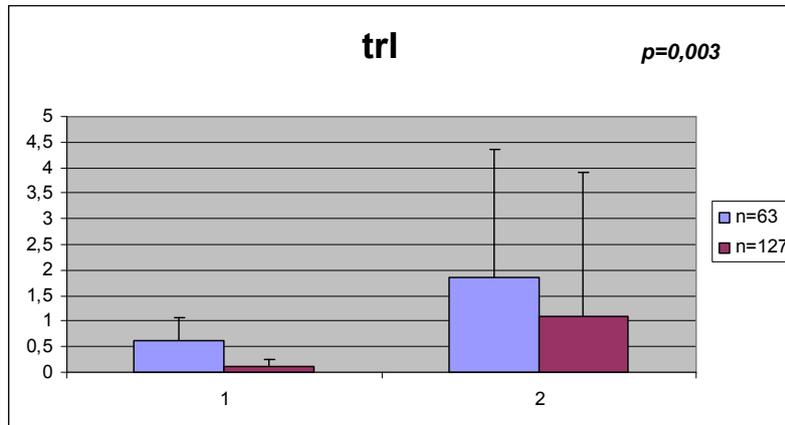


Figure 7/A

Serum CK and CK-MB levels (U/l) at the end of the operations (sample-1), on the first (sample-2), and on the second (sample-3) postoperative day



■ =CPB-CABG

■ =OPCAB

Figure 7/B

Serum cardiac troponin levels ($\mu\text{g/l}$) at the end of the operations (sample-1) and on the first postoperative day (sample-2)

The conclusion is clear, the OPCAB method is significantly better for preventing myocardial injury during the operations.

4.2

Life-saving arterial cannulation for emergency operations in acute proximal aortic dissection

Beyond all questions, in cardiac surgery, as well as in emergency patient care in cardiology one of our quality indicators is the success rate in the treatment of acute aortic dissection. When such a situation is suspected, unnecessary delay is the first possible mistake, which may be the cause of subsequent unsuccessful patient management (PUBL. 9).

Aortic dissection is an extremely diverse disease in terms of its main features. Unfortunately, it is not uncommon that by the time of the first available emergency intervention we are already late. Luckily, dissection itself is relatively rare, surgeons in each cardiac surgical center operate on one or two patients with dissection per month in average. But due to this rare occurrence that individual patient and surgeon concerned are not very lucky. According to this sporadic incidence, the knowledge about the disease and its treatment options is not deep enough in some centers and among physicians of emergency chest units, cardiologists and cardiac surgeons. The diversity in the nomenclature of the disease decades after the first successful repair, reflects the lack of protocols in patient management strategy. For correct decision making the exact diagnosis is essential. It is absolutely impossible to discuss the actual conditions of the patient, when the radiologist uses for example the DeBakey classification for evaluating the CT scan, the referring cardiologist uses the Stanford classification and the surgeon on the other end of the telephone line expects information about the aortic arch. But to solve this misunderstanding in diagnostic referrals is probably the easiest thing to solve in the management of aortic dissection.

The treatment focusing on classification contains only two terms: the *proximal* and the *distal* location of the pathology. The border between them is the isthmus of the aorta. It means that if any pathological changes occur in the wall of the ascending aorta, the aortic arch or the great arteries originated from that part of the aorta, the aortic dissection is proximal. In all other cases the aortic dissection is distal. There is another feature of the disease that helps with correct decision making, which provides much more possibilities for successful patient care management: the timing. If the occurrence of the dissection is within 24 hours it is acute, within 3 days it is sub-acute, otherwise chronic. If the patient has severe malperfusion in at least one vital organ or severe bleeding due to the dissection, an acute intervention is the only possibility for surviving. The above-mentioned diagnostic features are helpful in planning the operative details. Most patients have a relative time-window after the onset of the aortic dissection. The native courses of the disease are very different in terms of the main characteristics: the location of pathologic changes and the timing. *Acute* and *sub-acute proximal* aortic dissection is in itself a life-threatening situation. This behavior is based on a large number of observations. In contrast, *chronic distal* aortic dissection itself very rarely causes life-threatening sequels. The adequate patient care management in case of acute or sub-acute proximal aortic dissection is the emergency and in the latter, urgent intervention, mainly surgical. This is the most powerful hope for the patient and a big challenge for the surgeon who performs this type of operation relatively rarely.

One of the early obstacles during the operation is the need for quick and safe institution of CPB. Usually, the arterial cannulation is the most problematic step. Arteries in the groin may allow faster work, but using this port the CPB can be terrible itself. The reverse flow has unpredictable consequences in the often calcified descending aorta and also in the false lumen which sometimes becomes closed owing to the surgeon's mistake with cross-clamping the proximal part of the aorta. Using the axillary or subclavian arteries extrathoracally, or the distal part of a great side branch of the aortic arch in the chest cavity, even a non-dissected part of the proximal aorta are better options. But undetected or tardily detected malperfusion of the brain and/or severe aortic insufficiency may cause fatal consequences (PUBL. 10). If there is a suspicion

that for some reason the above-mentioned arterial cannula positions are all dangerous, the apex of the left ventricle provides the only life-saving solution. The apical cannulation requires a special, but commercially available arterial cannula. Since the heart is approached from median sternotomy the elevated position for the pipe insertion may cause circulatory collapse. Before the apical cannulation it is useful to insert at least one venous cannula to allow immediate CPB starting. Transpositioning the arterial cannula from the apex into the reconstructed part of the aorta before weaning off bypass is recommended.

I performed successful CPB for cooling with apical cannulation in three cases, and we published these results in 2004 (PUBL. 10).

4.3

Long-term left ventricular assist device therapy

There are three types of long-term MCS systems including also left ventricular assist: the bridge-to-transplant, the bridge-to-recovery and the destination therapy.

Bridge to transplant (BTT)

It means using mechanical assist systems with the goal of bridging to heart transplantation. Since the late 1980s, this method has been used successfully to support an increasing number of patients until a suitable donor organ became available. During the bridging period which ensures almost normal circulatory status, impaired organ function due to previous cardiac insufficiency can be resolved, thus giving a better overall condition for the expected transplantation.

By now, this "bridging period" has been gradually extended from days to a few weeks, then to some months up to years due to the shortage of donor organs and increasing demands.

With mobile ventricular assist systems patients can return to near normal lives, some of them to professional activities.

Risks such as infections, thromboembolic events, bleeding complications and mechanical failures naturally also increase with time on the device.

The stagnating number of transplant procedures and the dramatically prolonged waiting periods on the device demonstrate the limited success of the BTT hypothesis.

Patients are now waiting in hospitals, rehabilitation clinics or at home for their "donor heart", but the waiting list of BTT is growing and patients are now dying while on the list.

Bridge to recovery (BTR)

At first MCS systems were used in post-cardiotomy heart failure until adequate recovery of patients' myocardium occurred or short term negative side-effects of the surgical repair were overcome. BTR candidates were thought to be limited to post-cardiotomy VAD implants.

Today, mounting evidence exists to support the hypothesis that the temporary use of VAD systems may allow for the recovery of native heart function in other cases of insufficiency.

In recent years VAD patients afflicted by post-partum, viral cardiomyopathies and even ischemic heart disease were successfully weaned from mechanical support.

Destination therapy

Assist-systems, working in parallel with the natural heart still in place, are less complex and safer, in most patients the remaining pumping function of the heart will keep the patient alive, even in case of technical failure, until the problem is solved. Left ventricular support for acceptable life prolonging durations is feasible with some of present-day existing systems. The HeartMate XVE LVAD, which has been in use in some form since the early 1980s, was approved for clinical use as destination therapy by the FDA in 2002. Even axial-flow LVADs, such as the Jarvik 2000 and the HeartMate II, show the potential to be used as permanent long-term therapy.

The most appropriate cannulation sites for LVADs are the apex of the left ventricle and the aorta. Present-day existing devices, which can be used with **apical cannulation** are the following:

Pulsatile, paracorporeal systems

Pulsatile systems emulate the heart's natural pulsatile blood flow with periods of rest (filling) and work (emptying). Many ingenious methods have been developed to provide pulsatile flow from a mechanical pump. Pulsatile systems have valves, which provide unidirectional flow. The work of squeezing a flexible blood sac or moving a membrane is accomplished either with compressed air, mechanically with an electromechanical motor or hydraulically with an electrohydraulic pump.

The **BVS 5000 VAD** (ABIOMED, Inc.) is a pneumatically driven, pulsatile extracorporeal, asynchronous pump that can be used for left ventricular, right ventricular, or biventricular support. The device is used primarily as a BTR. The BVS 5000 system consists of a dual-chamber blood pump, cannulas, and a drive console. The device is positioned at the patient's bedside and fills passively by gravity. A bladder within the ventricular chamber is collapsed by pulsed air delivered through the drive-line tubing connected to the external console. The BVS 5000 can produce a stroke volume of 80 ml and flows of up to 6 l/min.

The **AB5000** circulatory support system (ABIOMED, Inc.) is similar to the BVS 5000, in that it uses the same drive console and tubing, but different in that its prosthetic ventricle consists of a membrane and 2 trileaflet valves. The indications for its use are the same as those for the BVS 5000. Like the BVS 5000, the AB5000 can produce a stroke volume of 80 ml and flows of up to 6 l/min.

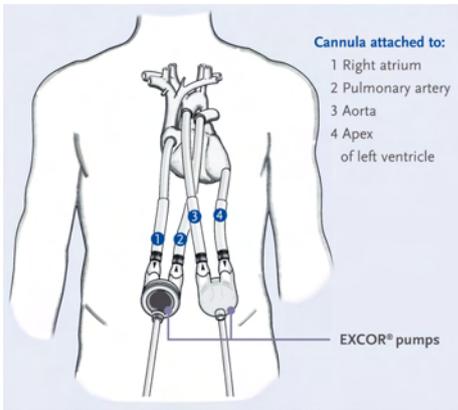
The **Thoratec paracorporeal** ventricular assist device (PVAD) system (Thoratec Corp.) is a pneumatically driven pump that can provide either univentricular or biventricular support. Indications for the Thoratec PVAD include acute heart failure, postcardiotomy shock, and BTT .The system consists of one or two blood pumps,

inflow and outflow cannulas, and a drive console. The external pump and the cannulas rest on the abdomen and connect to the drive console via pneumatic and electric drive-lines. The pneumatic console provides alternating negative and positive air pressure that cause the pump's blood sac to fill and eject blood. The pump can produce a stroke volume of 65 ml and flows of up to 7 l/min.

The **Berlin Heart EXCOR®** is a paracorporeal pulsatile VAD (Figure 8). By offering a wide range of different sizes and types of blood pumps, a manifold variety of atrial, arterial and apex cannulas and a stationary, as well as a mobile driving unit, it covers all clinical requirements.

Every EXCOR® blood pump consists of a transparent polyurethane housing that is divided into one air chamber and one blood chamber by a three-layer membrane. Graphite between the membranes helps to minimize friction. The membrane on the blood side merges seamlessly into the surface of the housing. A specially produced CARMEDA® coating is plated on the blood contact surface. In- and outflow sockets, which are made of polyurethane and bear titan connectors for the connection of the cannulas, lead from the blood chamber to the inlet or outlet cannulas. On the air side of the membrane lies the connection for the pneumatic driving tube.

The Ikus driving unit is designed for the stationary use of EXCOR® and EXCOR Pediatric® blood pumps. Ikus meets all requirements regarding frequency of the pump, synchronous and alternate mode as well as varying driving pressure. While in biventricular operation, both blood pumps can be controlled separately. A laptop with an installed monitor program is integrated into the Ikus housing and all parameters can be adjusted and viewed.



EXCOR® VAD System

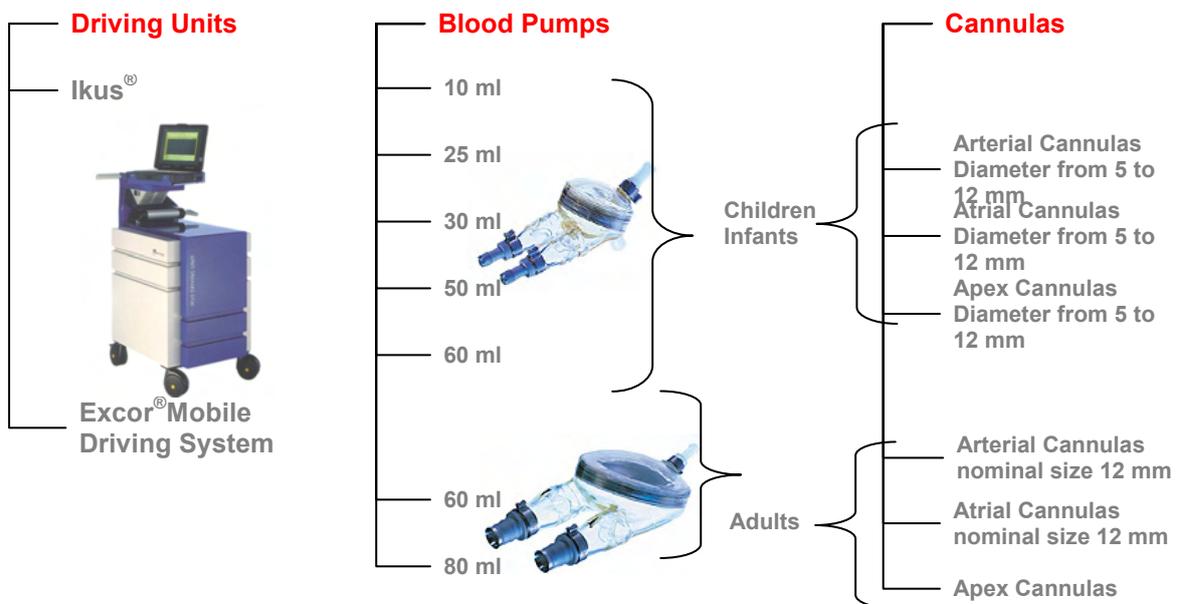


Figure 8

Scheme of EXCOR® BiVad; different size apical cannulas; details of the system (source: Mechanical Circulatory Support Systems Workshop at the Deutsches Herzzentrum Berlin, November 5-7, 2007)

After my successful training abroad, on 16 June 2008, I was charged with organizing the long term MCS program at my workplace, the Gottsegen György Hungarian Institute of Cardiology.

Between 29 September and 1 November 2008 we performed the first successful BTT therapy with an EXCOR® Bi-VAD in a girl of 2.5 years of age with a body weight of 10 kgs in Hungary (PUBL. 11) (Figure 9).



Figure 9

/A: Patient on Bi-Vad

/B: Patient after HTX

For better infection control, we applied standard dressing regularly, the steps of it are shown on Figure 10.

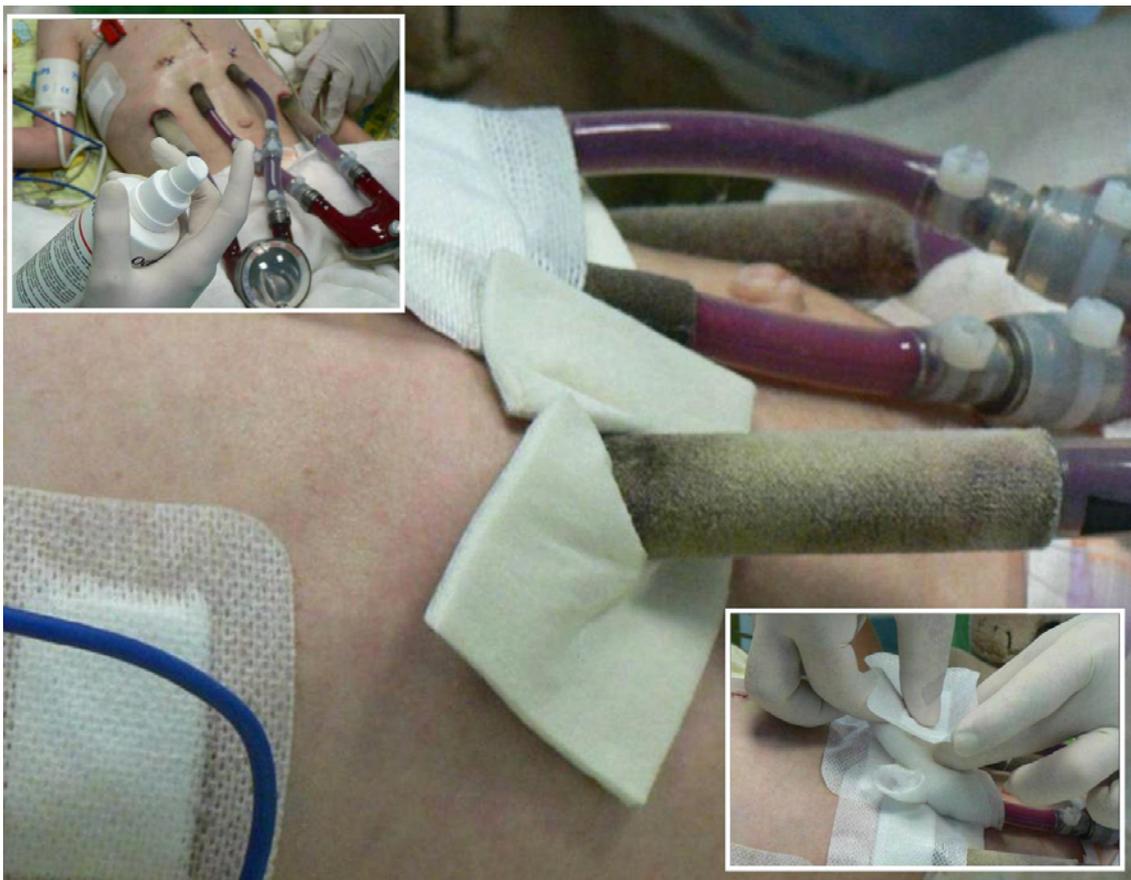


Figure 10

The steps of standard dressing for better infection control

For appropriate anticoagulation management, we provided bedside possibility of thrombelastography and aggregometry (Figure 11), and performed visual pump-control regularly (Figure 12).



Figure 11:
 Bedside thrombelastograph and aggregometer first time together for supporting MCS therapy in Hungary

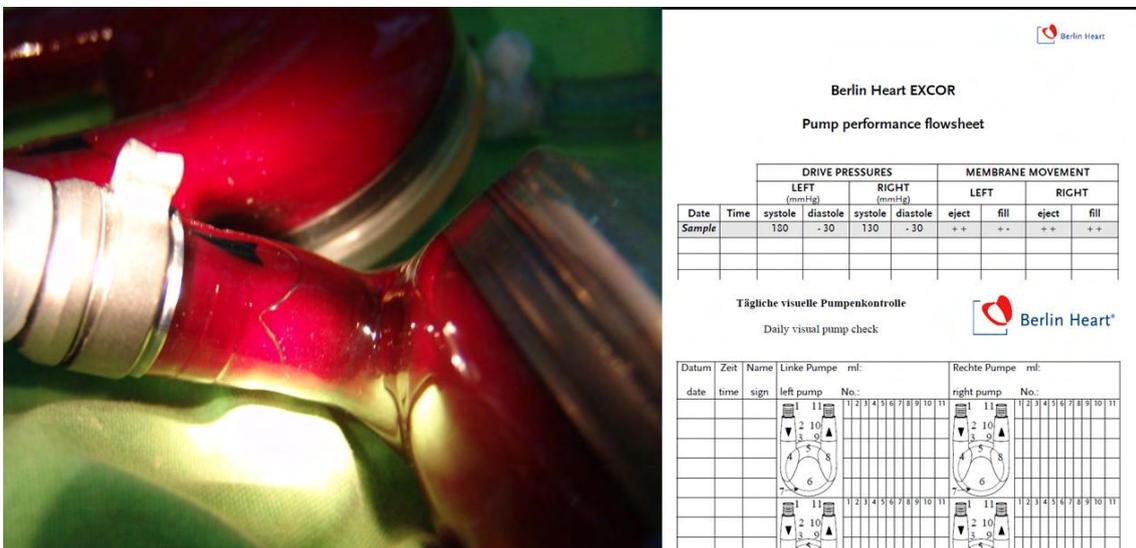


Figure 12:
 Lights for midnight pump-control and sheets for documentation

Pulsatile, implantable systems

A modified PVAD **Thoratec P-IVAD** (Thoratec) has been introduced as an implantable version that can be used as a univentricular (left or right side) or biventricular support system for intermediate or long-term implantation. This version reduces the number and size of skin penetrating tubes, thus reducing the risk of infections. The larger bore arterial and atrial cannulas are shorter and kept inside the chest.

The HeartMate **HeartMate® IP** implantable pneumatic left ventricular assist system (HeartMate IPLVAS, Thoratec Corp.; Pleasanton, Calif.) is a pulsatile blood pump that provides left ventricular support. The HeartMate IP is used in patients as a BTT or BTR. The system consists of a pusher-plate blood pump, an interconnecting drive line, and an external drive console. The pump is positioned in the upper left abdominal quadrant, either intraperitoneally or preperitoneally. A percutaneous drive line attached to an external console delivers pulses of air that cause the pusher-plate and diaphragm to eject blood from the pump. A sensor, located in the lower housing of the blood pump, monitors the position of the diaphragm in order to determine the stroke volume. The pump can produce a stroke volume of 83 ml and flows of up to 11.5 l/min.

The HeartMate **HeartMate® VE and XV E** vented electric LVAD (HeartMate VE LVAD; Thoratec Corp.) and an improved version called the HeartMate extended vented electric LVAD (HeartMate XVE LVAD) are very similar to the HeartMate IP LVAD.

The main difference between the IP device and the VE devices is the method of actuation. The HeartMate XVE is driven by an internal motor that requires 12 V of direct-current power. The motor controls the pusher-plate and diaphragm within the

pump. This system is used as a BTT, as a BTR, and as destination therapy. A percutaneous drive line attaches to a controller, which connects to a power base unit. The drive line also has a percutaneous vent tube, the purpose of which is to equalize the pressure in the motor chamber thus avoiding an internal compliance chamber. The HeartMate XVE can be powered for short periods (4–6 hours) by portable batteries, thus providing a distinct advantage over the pneumatic version and allowing more patient mobility.

In light of the encouraging results of the multicenter REMATCH trial, which compared LVAD therapy and optimal medical management in patients ineligible for cardiac transplantation, the FDA approved another slightly modified version of the pump, the HeartMate® SNAP-VE, as destination therapy. In 2003, the HeartMate XVE LVAD was also approved by the FDA as destination therapy.

WorldHeart's **Novacor® LVAD** is an implanted, wearable system that provides pulsatile circulatory support for patients with life-threatening heart failure. Novacor® LVAD is the first MCS device to support a single patient for more than six years. Novacor® LVAD is an abdominally implanted, electro-magnetically driven pump. Blood enters the Novacor® LVAD pump through an inflow conduit connected to the recipient's left ventricle. The pump ejects blood through an outflow conduit into the arterial system, thereby supporting the systemic circulation. The system is completely self-regulating, automatically adjusting its beat rate and stroke volume in response to the recipient's changing circulatory requirements. The external Controller is connected to the implanted pump by a percutaneous lead - a small tube that brings control and power wires through the recipient's skin. The Controller regulates the pumping action of the LVAD, and monitors system function. During normal operation, the Controller receives power from two rechargeable power packs. The Controller and Power Packs may be worn on a belt or carried in a shoulder bag, vest or backpack. The portable nature of the Novacor® LVAD facilitates out-of-hospital use and allows recipients to return home and lead near-normal lifestyles.

Non-pulsatile, axial flow systems

The **MicroMed DeBakey VAD®** is a miniature axial flow heart pump or VAD (VAD) designed to provide increased blood flow (up to 10l/min) from the left ventricle of the heart throughout the body for patients who suffer from end stage heart failure. About 1/10 the size of competitive pulsatile VAD products on the market and weighing less than 95 grams, the MicroMed DeBakey VAD® measures 1" x 3" (30mm X 76mm). This size gives a treatment hope to tiny women and children because larger devices cannot be implanted in them. The small size of the device and flexible percutaneous cable should also provide lower infection rates.

The DeBakey VAD® is the only implantable VAD with a flow probe that directly measures blood flow through the pump. The DeBakey VAD® contains only one moving part, the inducer-impeller which is supported by a patented ceramic bearing system with years of proven durability.

The **Thoratec HeartMate® II LVAD** is a high-speed, axial flow, rotary blood pump. As an axial flow device, the HeartMate II produces no pulsatile action (Figure 12). It is significantly smaller than other currently approved devices. As such, it may be suitable for a wider range of patients, including small adults and children. The HeartMate II is being evaluated initially for use as a bridge to transplantation. Eventually, it has the potential to be used for destination therapy—as permanent support for end-stage heart failure patients who are not eligible for heart transplantation.

The internal pump surfaces are smooth, polished titanium. The blood path is biocompatible and designed to avoid hemolysis. The textured titanium surfaces are thromboresistant. Within the pump is a rotor that contains a magnet. The rotor assembly is rotated by the electromotive force generated by the motor. The rotor propels the blood from the inflow cannula out to the natural circulation. The pump speed can vary from 6,000 rpm to 15,000 rpm, providing blood flow of up to 10 liters per minute.

The **Berlin Heart INCOR®** pump is made of titanium and is only 12 cm long, its diameter is 3 cm and it weighs 200 g. Inside the pump, a rotor rotates in a range

between 5000 to 10000 rpm. This axial rotor is solely held in position by magnetic bearings. Due to the magnetic suspension, there is no friction and thus no generated heat. Theoretically, the pump can run endlessly. The blood coming from the heart flows into the axial pump and passes the inflow guide vane. An outflow guide vane behind the rotor then takes spinning movement out of the blood, additionally building up pressure and channels it through the outflow cannula into the aorta. The necessary electricity for the pump driver is conducted through a small cable, which is lead through the skin on the right side. The cable is connected to a small control unit. The control unit monitors and controls the entire system. Connected to the control unit are the main and the reserve batteries, which supply the system with electricity.

For these systems, high quality **apical cannulation** is the most appropriate solution for pump filling in long-term application. There are two novel devices – the axial flow **Jarvik 2000[®]** and the radial flow **HeartWare HVAD[™]** without any filling cannula. In these systems the **pumps itself are implanted into the apex** of the left ventricle.

The MCS therapy has arrived into a new “golden era” with these above-mentioned systems in recent years. Among the landmarks, which made this possible (better infection control, appropriate anticoagulation management, smaller size, etc.), the usage of the **cardiac apex** for these innovative implantation techniques is one of the most important.

4.4

Alternative method for cardiac resynchronization: transapical lead implantation

CS lead placement for transvenous left ventricular pacing in CRT has a failure rate at implant and at short-term follow-up of 10% to 15% (26). The most frequently used alternative for these patients is epicardial pacing lead implantation. Recent data support endocardial lead implantation through the atrial septum and the mitral valve because this method provides further hemodynamic advantages (27, 28). Transseptal CRT carries a significant risk for device related infective endocarditis of the mitral valve, this condition can be treated only with a very high-risk surgical lead extraction and repair or replacement of the valve (PUBL. 12). There is a fundamentally new approach of using transapical implantation of an active fixation endocardial pacing lead. This technique is based on a direct puncture of the left ventricular apex using the standard Seldinger technique. The tip of the lead is positioned with intracavitary navigation under fluoroscopy. This method offers advantages for cardiac resynchronization because it is minimally invasive, provides endocardial pacing and does not involve the mitral valve (PUBL. 13, 14, 15).

The first application direct puncture of the ventricle was performed not in therapeutic but diagnostic procedures in heart diseases. Using this type of puncture to administer radiopaque contrast material into the cardiac ventricles was described by Raboult in 1933. Clinical experiences with the procedure began to accumulate after 1957, when Lehman described it as a part of the study of cardiac disorders (29). The patient was placed in the supine or in the right posterior oblique position on top of a rapid cassette changer. A 17-gauge, 18 cm long, thin-walled Lehman needle with a single side hole was introduced percutaneously into the heart. In case of adults local, whereas for children general anesthesia was employed. In order to determine the position of the

needle they applied continuous oscilloscopic monitoring. The most important and otherwise not achievable details were provided by the left ventricular angiography, so in the beginning the vast majority of the direct punctures targeted the apex of the left ventricle. It sometimes caused undesirable sequels, such as pneumothorax or injury of the left coronary artery. Because of this unsatisfactory experience the pioneers of cardiac catheterization changed their method. They inserted the needle at the subxiphoid and by directing it through the apex of the right ventricle into the septum and then the left ventricle, lessened the hazard of injury to the left coronary artery or of entering the pleural cavity that was associated with direct left ventricular apical puncture. Lead markers were placed over the area of the heart and an additional lead marker was positioned at the xiphoid process. The passage of the needle was through the apex of the right ventricle, into the septum and then the left ventricle, so the monitor first showed a right ventricular curve that became damped as the needle passed through the septum and then the typical left ventricular tracing when the needle entered the cavity of the left ventricle. The direct left ventricular puncture as an adjunct to cardiac catheterization was at the time the only possibility in quantification of mitral insufficiency, visualization of the left ventricular outflow tract, demonstration of ventricular aneurysms, visualization of the thoracic aorta and the brachiocephalic vessels, and measurement of aortic and mitral gradients. When less invasive techniques were developed to study these features of cardiovascular abnormalities, direct punctures of the ventricles disappeared from the catheter-laboratories; but they remain in the memory of my honored emeritus professors.

Before the development of CRT to treat DCM caused heart failure different types of pacemaker and ICD therapies were already in use for treating cardiomyopathies and their consequences. For patients suffering from hypertrophic obstructive cardiomyopathy the AV sequential pacing with short AV delay to reduce left ventricular outflow tract pressure gradient has an advantageous effect. The implantable cardioverter defibrillator was the first treatment option that brought forth a significant improvement in the survival of sudden cardiac death due to ventricular tachyarrhythmias, this otherwise less treatable life-threatening consequence of different types of

cardiomyopathies. Multisite pacing was not yet performed to achieve only intra- or interventricular resynchronization. The goal of bi-atrial pacing was to manage atrial tachyarrhythmias, whereas the four chamber pacing was developed to manage independent AV sequence for the left side of the heart. The beneficial effect of bi-ventricular pacing as part of multisite pacing on the left ventricular function was initially an unexpected result. This type of multisite – and of course also bi-ventricular – pacing was performed with epicardial electrodes in most of the cases. The CS lead was used more frequently for left atrial pacing that time. After recognizing the importance of bi-ventricular pacing in heart failure in patients with permanent atrial fibrillation as well, the CS and its ventricular side branches became the primary target for left ventricular leads. The following configuration of the electrodes is the gold standard of CRT: right ventricle, CS-left ventricle and right atrium if chronic atrial fibrillation is not presented.

All the details of implantation technique, of the best locations of the electrodes regarding the respective chambers, of the most beneficial pacing algorithms were evaluated and re-engineered several times in the brief twenty years history of CRT. Any standard type of the previously used ventricular or atrial pacing leads can be placed into the CS. It happened accidentally several times in the past, and in most cases suboptimal pacing and sensing parameters were achieved. Physicians made great efforts to prevent placing the lead in this “unacceptable position”: the CS. “Tempus fugit” and those physicians – including myself – spent ours in the operating room or catheter-laboratory locating the orifice of the CS and trying to achieve mechanically fixed and electronically accepted position for the tip of the left ventricular electrode without stimulating the left phrenic nerve. The right atrial and right ventricular electrode positioning were also evaluated. The best position for the tip of the right atrial electrode remained the right atrial appendage. This position provides an excellent mechanical fixation also for passive fixation leads, intra- and interatrial conductions are not deteriorated by unacceptable delays. The septal or apical placing of the tip of the right ventricular electrode remained controversial, since it depends on other issues, for example the leading algorithm behavior of the system. Basically there are two main

choices: implanting a cardiac resynchronization system with only pacing possibilities, or also with ICD features. These systems are called CRT-P and CRT-D respectively. In CRT-D implantation the tip of the right ventricular lead is positioned preferably in the apex since this lead provides also the main defibrillator electrode. The most appropriate position of this part of the lead can be achieved when the tip is located in the apex. CRT-D system implantation or upgrade is indicated when these two features are indicated separately. Currently, this is the most sophisticated cardiac rhythm management system that can be implanted also by using endovenous way for every leads.

A special subcutaneous lead can also take part in these systems when endocardial leads and the external surface of the generator do not provide optimal solution for defibrillation.

The standard technique with excellent supporting devices was recently developed for implantation of a totally endovenous cardiac resynchronization system using the tributaries of the CS for left ventricular lead. Regardless of this well-standardized procedure the CS route does not provide acceptable results for lead positioning in a significant number of patients. Intubation of the CS could be problematic due to anatomical abnormalities of its orifice. The other problematic situation is when the anatomy of the side branches causes difficulties for optimal electrode positioning. For instance, there is no acceptable posterior or lateral side branch, all of them are either too small or too large for making the insertion and/or fixation the tip in the optimal distance from the apex difficult. The phrenic nerve stimulation can create an unmanageable situation associated with an elevated pacing threshold. The elevated pacing threshold in connection with the CS electrode could also be a frequent problem itself.

To solve these problems is mandatory to provide beneficial effects of CRT for these patients. Historically there is a well-known method to achieve direct electrical connection with the ventricles. It is the epicardial implantation of the pacing lead which was performed frequently after the first permanent pacemaker system implantation in 1958. Following the technological improvements in pacing lead manufacturing the vast

majority of the electrodes is implanted endocardially, but in some rare situations (e.g. native or post surgical tricuspid abnormalities, Fontan circulation, small vessel and heart size in children) there is no other option for ventricular pacing than epicardial implantation. Fortunately, the technological development had favorable effects on epicardial leads too. These modern epicardial electrodes are also used for left ventricular pacing in resynchronization therapy if the CS approach fails. To determine and plan the position of these left ventricular epicardial electrodes for CRT is not too difficult, but the successful implantation depends on some unexpected details. Due to left ventricular dilatation, reaching the target area and pacing the most delayed segment of the lateral wall can be difficult or in some cases even impossible. Pericardial adhesions, that might be fairly common in this group of patients, can hide the location of epicardial coronaries. It is a challenging process to avoid damaging important vessels whilst inserting the epicardial lead. Unfortunately, in some centers the implanting surgeons are not familiar with CRT, therefore the importance of the lead postero- or postero-lateral or lateral and basal- or mid-ventricular positioning is pushed into the background during the implantation. Moreover, the main limitation of the standard epicardial lead implantation is the invasiveness of this method in comparison with the endovenous implantation.

The latest surgical technologies provide less invasive implantations with video assisted and/or robotic methods (30), on the other hand these techniques assume extra instruments and experiences.

To achieve less invasive and less expensive alternatives for patients without acceptable CS route different endovascular implantation techniques have been developed (27, 28). The avoidance of surgical assistance also seems to be an additional tempting effect of these methods so the whole procedure remains in the invasive cardiologist's hands in the catheter-laboratories.

The idea is partly originated from the accidental implantation failures in the past (31, 32, 33), when e.g. the leads passed through an open foramen ovale and the left AV orifice – the mitral valve – and finally fixed in the left ventricular endocardial surface. In other cases the subclavian puncture targeting the vein was missed and the lead got into the arterial system, passed the aortic valve and fixed in the left ventricular endocardium. The consequences of these unrecognized malpositions were terrible in some patients when thromboembolic events occurred related to the left sided part of the leads without any anticoagulation. To keep the implantation on the endovascular side efforts were made with both mechanisms. Fortunately, the retroarterial route passing the aortic valve is still in the experimental phase (34). Acceptable results without any damaging effect on the valve itself are still to be expected from animal studies.

The trans-septal implantation of the left ventricular lead as a planned therapeutic method has already been performed for a decade (27). Having gained sufficient experience with this type of resynchronization therapy the otherwise theoretical issue, that the endocardial pacing is more beneficial than the epicardial one (both from the CS and from the epicardial surface) was finally proved (35, 36, 37). An activation sequence originating from the endocardial surface has advantages over epicardial stimulation. Endocardial stimulation has shown to be associated with a greater aortic and mitral time velocity integral, an increased left ventricular fractional shortening and an improvement in the regional electromechanic delay in comparison with epicardial stimulation. Regarding this beneficial effect, the number of responders for CRT could be increased, but the possible undesirable side effects are also on the horizon.

Importance of the activation sequence originating from the endocardial surface:

It is interesting and slightly amusing that some scientific experts of CRT do not take account of the activation sequences originating from the outer surface of the ventricle or from the inner surface, such as the physiological sequence. For better and energy-effective performance of the myocardium it is essential that the contraction of the endocardial part should come first followed by the contraction of the epicardial part, and of course the relaxation of the endocardial part comes behind the relaxation of the

epicardial part. This mechanical-physiology is well shown in the electro-physiology, and recorded on every physiologic surface ECG strip: the main vectors of ventricular depolarization and repolarization are the same. It means that the physiologic pacemaker and conduction system provides electronic signal first on the endocardial surface to be able to start contraction endocardially. After that, the electronic changes of myocytes provide delayed repolarization endocardially to be able to start relaxation in the outer myocytes. This physiology fails in its first part when artificial pacemakers and conduction systems deliver electronic signal to the outer surface of the ventricle. Traditionally, when physicians implanted artificial pacemaker systems surgically in that approach the outer surface of the heart was directly involved – both on the right and on the left side. In the case of standard endovenous implantations of antibradycardia and/or defibrillator rhythm management systems the leads are connected to the endocardial surface of the right side chambers of the heart. The most frequent consequences of these highly preferred implantation techniques in the activation sequence of the LV wall are the following:

- a) endocardial pacing in the right ventricle and intact intraventricular conduction system (Purkinje fibers, Bundle Branches) – LV activation sequence from the endocardial surface
- b) endocardial pacing in the right ventricle and failed intraventricular conduction system – random LV activation sequence
- c) epicardial pacing in the right ventricle and intact intraventricular conduction system – LV activation sequence from the endocardial surface with good chance
- d) epicardial pacing in the right ventricle and failed intraventricular conduction system – random LV activation sequence
- e) epicardial pacing in the left ventricle and intact intraventricular conduction system – LV activation sequence from the epicardial surface at least around the electrode
- f) epicardial pacing in the left ventricle and failed intraventricular conduction system – LV activation sequence from the epicardial surface.

The possible variations are not limited to these six options. These are only trends to show correlation between pacing site and activation sequence in the LV wall. The consequences of this correlation are also influenced by some other variables. In most the

cases with classic indication these features are more important predictors of the optimal rhythm management than the LV wall activation sequence itself. A complete atrio-ventricular block with critical bradycardia could be successfully treated with left ventricular epicardial pacing as well: avoidance of the life-threatening asystole is more important than the consequences of pathological activation sequence around the electrode. Therefore, it is not surprising that generations of physicians did not show interest in the exact mechanism of cardiac pacing. They traditionally consider and name all endovenous implantations as endocardial pacing and all surgical implantations as epicardial pacing regardless of the real activation sequence in the LV wall. Even leading electro-physiologists shared this misunderstanding in 2005 (38), seven years after the first real endocardial LV pacing for CRT was published.

It should be made clear that LV leads in the CS are not endocardial and do not provide LV activation sequence originated from the endocardial surface. These leads – and of course all surgically implanted LV epicardial leads – pace the LV wall from the outer surface of the heart, and cause activation sequence originated from the epicardial surface. According to the failed intraventricular conduction system, in this group of heart failure patients who are candidates for CRT this pathological activation sequence appears not only around the electrode but it mainly involves the major part of the LV wall.

This greater mass of LV wall with pathological activation sequence indicates the importance of the following two well-described consequences:

Endocardial LV stimulation provides better LV hemodynamics proved by echocardiography, including tissue Doppler imaging

The article on these findings was published in 2001 (36). The authors investigated twenty-three patients who received CRT systems from March 1999 to March 2000 according to standard indication. Biventricular pacing was applied in fifteen patients with epicardial LV stimulation using CS LV leads (called “Epi Group”), and endocardial biventricular pacing with standard unipolar active fixation leads were placed via the transseptal approach into the LV cavity (called “Endo Group”). After about six months of stable biventricular pacing functional improvement was observed in all patients in both groups. The mean NYHA functional class decreased from 3.7 ± 0.5 to 2.6 ± 0.9 after CRT system implantation for the Endo group, and from 3.4 ± 0.6 to 2.7 ± 0.7

respectively for the Epi group. There were also significant shortenings in QRS durations in both groups.

Echocardiographic examinations were performed at that time. The patients were randomized to one day of right ventricular pacing or biventricular pacing with crossover.

The authors found statistically significant difference between the patients of the two groups in all hemodynamically relevant parameters – both measured with standard echocardiography and tissue Doppler imaging – when compared the changes between the right ventricular pacing (baseline) and biventricular pacing. For statistical analysis quantitative variables were assessed by the authors using the analysis of variance design with repeated measurements for the same patients. The exact (nonparametric) Fisher's test was performed for qualitative variables. The Spearman's coefficient was used to quantify and to assess the correlations between the quantitative variables. A p-value of less than 0.05 was considered significant. The power of these statistically significant differences is increased by the fact, that the baseline data (with right ventricular pacing) were statistically similar between the two patient groups. All differences proved beneficial effect of endocardial LV pacing as part of biventricular pacing over the epicardial LV pacing from the CS.

In details, measured with standard echocardiographic methods increase in percentage of the aortic and mitral time-velocity integral, the aortic maximal velocity, and the LV shortening fraction was significantly greater in the Endo group than in the Epi group with biventricular pacing. Additionally, the aortic preejection interval was even shorter with endocardial than with epicardial LV stimulation during biventricular pacing.

The tissue Doppler imaging echocardiographic technique also showed beneficial effects on the endocardial LV stimulation side. As described by the authors, these measurements were performed using the pulsed Doppler mode. Acoustic power, gain, dynamic range, and filters were set for each myocardial area analyzed with right ventricular pacing and biventricular pacing. The Doppler window was changed only after complete recordings were obtained for both modes to analyze exactly the same myocardial segment with the different pacing modes. The explored areas were the basal septum and the basal free wall. From the Doppler spectrum the authors quantified two variables in the two examined myocardial area:

- *peak velocity of the S-wave* as corresponding to the systolic motion of the LV wall with regard to the Doppler cursor,
- *electromechanical delay* defined as the time period between the stimulation spike on the surface ECG and the onset of the S-wave.

The S-wave amplitude was augmented more in the Endo group than in the Epi group, in comparison with right ventricular pacing ($+69.7 \pm 11.8\%$ vs $+4 \pm 1.2\%$ for the septal wall, $p < 0.001$, and $+31.2 \pm 7.8$ vs $+13.5 \pm 3.9\%$ for the free wall, $p = 0.013$, respectively). Endo group patients had significantly greater shortening of regional electromechanical delays of the LV septal and free walls than Epi group patients, compared with right ventricular pacing.

The results published in this article clearly proved that pacing the left ventricle from the epicardium – such as from a tributary of the CS – improves patients with severe heart failure hemodynamically, but in a lesser extent than endocardial pacing would do.

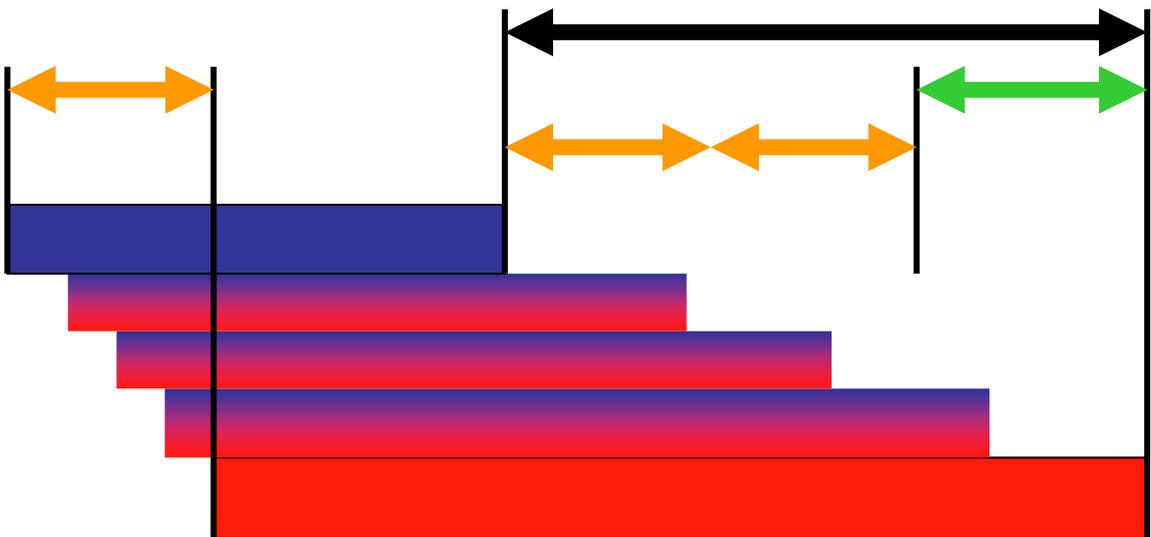
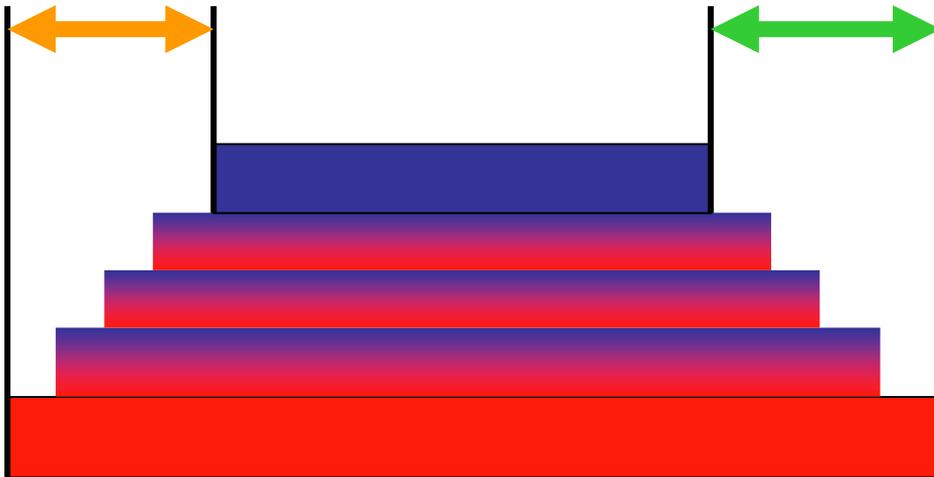
Epicardial LV stimulation increases the risk of ventricular arrhythmias

In the optimal mechanical performance of the ventricular wall the systolic part of the heart cycle is longer in the endocardial cells than in the epicardial cells, as it is also mentioned in the first paragraph of subchapter 5.4.1. Consequently, the physiological QT interval is shorter in the epicardial cells than in the endocardial cells. The difference must be greater than the transmural depolarization conduction time plus the time necessary for the step-by-step relaxation from the epicardium to the endocardium.

There is a simple mathematical consequence of this physiologic difference in endo-epicardium specific QT intervals on the summarized QT interval when depolarization starts from the epicardial surface: it has to be prolonged (Figure 14). Theoretically, it is easy to calculate this difference in the summarized QT intervals when activation sequence is changed from the endocardial origin to the epicardial origin: it has to be the endocardial QT interval plus the transmural depolarization time (in this case this latter one means the period lasting from epicardial pacing stimulus until depolarization occurs in the endocardial cells).

This theoretical example shows that there has to be a bigger difference in transmural dispersion of repolarization – the time period when already repolarized cells and still depolarized cells are present in the myocardium at the same time (green and black arrows on Figure 13). The role of this situation in arrhythmogenesis is also well-known.

ENDOCARDIAL PACING



EPICARDIAL PACING

 = endocardial QT interval,  = epicardial QT interval,

 = transmural depolarization time,  = transmural repolarization time,

 = prolonged transmural dispersion of repolarization

Figure 13

In addition to the theoretical basis of QT prolongation and arrhythmogenic effects caused by epicardial pacing, experimental and clinical data also prove these consequences (39, 40, 41).

In an experimental study (39) transmural ECG and transmembrane action potentials were simultaneously recorded from epicardial, intramuscular, and endocardial cells of arterially perfused canine LV wedge preparations. QT and JT interval increased significantly when pacing was shifted from endocardium to epicardium.

Another publication (40) includes experimental and also clinical data about the potential proarrhythmic effect of epicardial LV pacing. The authors presented increased QT interval and increased transmural dispersion of repolarization as a consequence of epicardial pacing in rabbit LV wedge preparations.

In this publication similar results were presented on humans. JTc and QTc intervals of 29 patients treated with CRT increased after LV epicardial pacing.

The authors also discussed ventricular arrhythmias after CRT upgrade that is clearly related to the epicardial LV stimulation performed by the CS lead.

Almost all the consequences of the effective CRT predict lower risk and occurrence of ventricular arrhythmias, but clinical data do not support these expected beneficial effects. According to a study (42) involving 52 patients with CRT upgrade from implantable defibrillator therapy CRT is not associated with a decrease in the frequency of ventricular arrhythmia or an appropriate device therapy despite the proven favorable ventricular remodeling following CRT. The most promising method to achieve this still missing beneficial consequence of CRT induced remodeling is to change the epicardial LV stimulation to endocardial LV stimulation (43).

Regarding these beneficial effects of endocardial LV stimulation with transeptally implanted leads the number of responders for CRT could be increased and the episodes of ventricular tachyarrhythmias could be decreased, but the possible undesirable side effects are also on the horizon.

Concerns about the long-term outcome of transseptal cardiac resynchronization therapy: What we have learned from surgical experience

When a foreign body enters from the right atrium into the left side of the heart and is in close and permanent contact with the mitral valve, it increases the risk of mitral endocarditis (PUBL. 12). Moreover, when it happens, the outcome is presumably even more deleterious than the potentially lethal right-sided pacemaker endocarditis. Although reports are not available on this subject, conclusions can be drawn from previous surgical experience.

Interestingly enough, more and more reports confirm that the number of device related infections show instantaneous growth in the past two decades (44, 45). The increase is especially high in device related infections in comparison with the number of implantations, particularly after 2000 (46).

Pacing system related endocarditis and its consequences are well described (47). The essential step of the treatment on the right side is the complete removal of the pacing system, which requires sometimes high-tech technology (48, 49). Having removed the foreign body, the disease can be treated with acceptable results by antibiotics, as in any other aetiology of right-sided endocarditis.

When an enormous mass of vegetation increases the risk of pulmonary embolization, the only safe procedure is the complete removal with open-heart surgery (Figure 14).

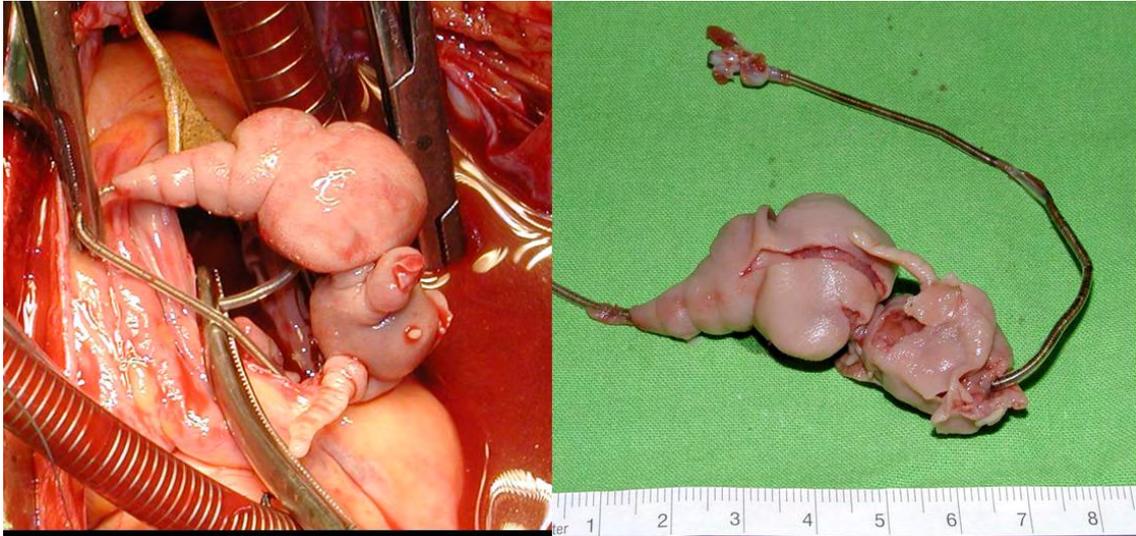


Figure 14

A: open-heart surgery
for complete removal

B: infected lead and the enormous
vegetation after removal

We, however, must emphasize that a significantly worse outcome is expected if the endocarditis involves the valves of the left side. This location of the disease would still mean high mortality and morbidity in spite of the novel treatment options as show by the most recent studies (50, 51). Furthermore, the consequence of septic embolization into the systemic circulation (brain vessels, coronaries, supplying arteries of parenchymal intra- and retroabdominal organs and gastrointestinal territory) can be fatal. Abscess formations in the target tissues and organs such as the brain, myocardium, liver, lien, kidneys, etc. are all very severe conditions that are simply not comparable with right sided pathologies. The obligatory anticoagulation therapy decreases the healing possibilities of these secondary infected, abscessed tissues (52). The infected mitral valve very often needs surgery itself. It is somewhat paradoxical, since most of these indications are based on the inoperability of the patient (27, 28).

Additionally, under these special conditions mitral valve surgery carries a higher risk for mortality and morbidity (53). We note that most of the transeptal implantations were performed as last remaining option for the patients.

There is a very sophisticated technique, developed in Hungary, to fix the CS electrode in place with a coronary artery stent when the too large side branch causes a problem. It can maintain the procedure on the endovascular way, but does not solve other difficulties and might bring some new problems if the removal of the lead is indicated.

A fundamentally new approach for endocardial left ventricular lead implantation

On this basis, we aimed to develop a fundamentally new approach for endocardial left ventricular lead implantation.

The patient should be prepared for the operation with general anesthesia using a regular intratracheal intubation and should be positioned for an infraclavicular incision as well as a small left thoracotomy. The apical process can be performed with video-assisted thoracoscopic surgery. However, in the latter case a selective bronchial intubation is needed and the port sites should also be included in the surgical field. Initial transthoracic echocardiography is used to locate the LV apex. The use of external defibrillator pads, placed antero-posterior is recommended.

Inside the chest, a small pericardiotomy is performed above the LV apex (Figure 15/A). Any type of standard active fixation endocardial pacing lead can be inserted in the LV cavity through the apex. We used one of the thinnest commercially available bipolar electrodes to reduce traumatic effect during insertion (Figure 16).

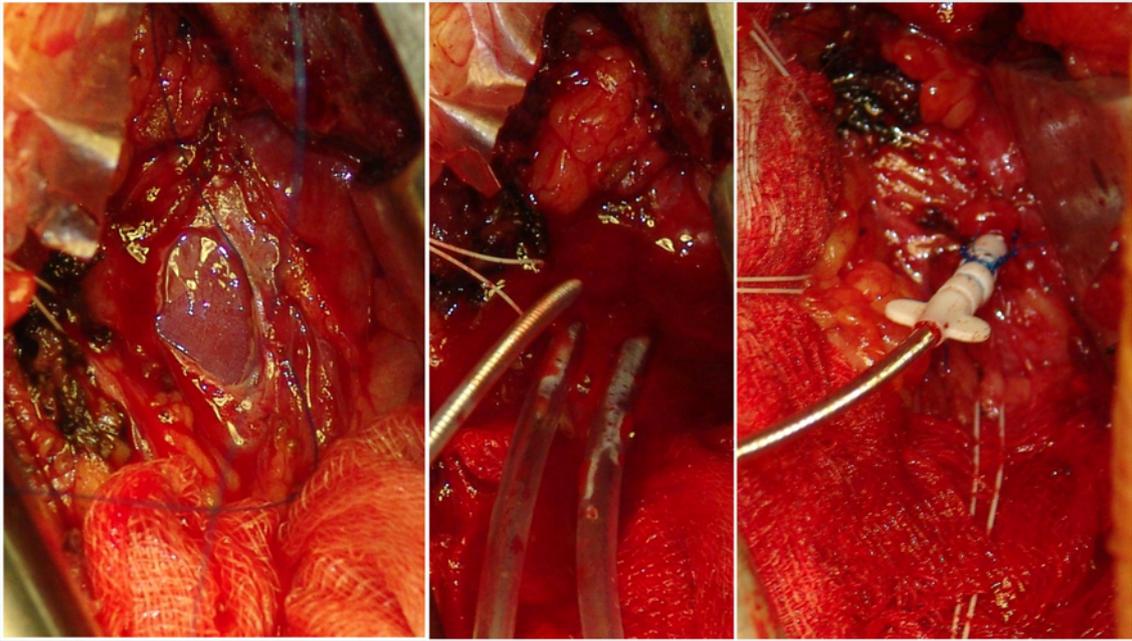


Figure 15

/A: pericardiotomy
just above the apex

/B: bleeding-control
with tourniquets

/C: fixation of the lead
at the apex

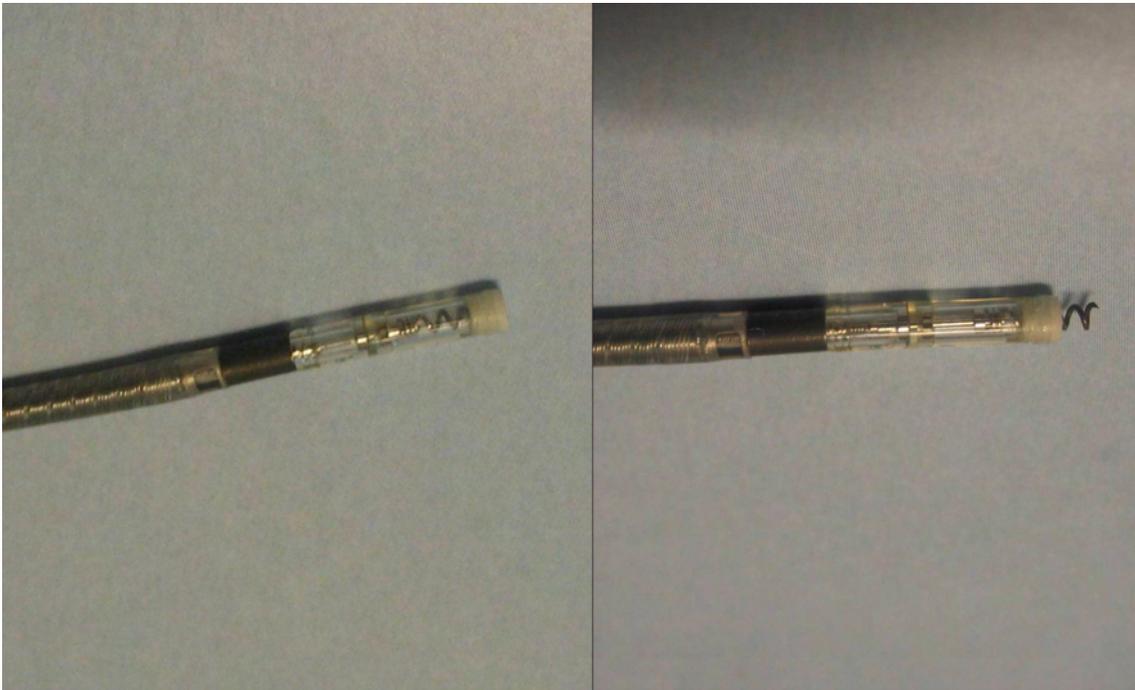


Figure 16

Photo of the lead tip with endpoints of the screw's movement

A standard Seldinger technique with a peel-away sheath is recommended for this procedure. When undertaking this procedure, the following steps should be followed: puncture the apex with a needle, insert the guide wire through the needle, remove the needle from the apex, dilate the apex hole with a peel-away sheath inserted over the guide wire, remove the guide wire, insert the pacing electrode into the LV cavity through the sheath and remove peel-away sheath.

Hemorrhaging from the left ventricle can be controlled with one or two 5/0 or 4/0 monofilament purse-string sutures around the puncture point. It is recommended to place the sutures before puncturing the apex, and to apply them as tourniquets (Figure 15/B). If the tissue quality of the apex requires pledgeted sutures, we recommend pledge material in the surrounding pericardium.

Fluoroscopy is necessary for the intracavitary navigation and endocardial fixation of the electrode at the optimal pacing site for CRT. To reach the target area, a “J” shaped electrode guide wire is useful. After effective endocardial fixation of the lead tip, the pacing and sensing parameters should be measured. The acceptable pacing threshold for this kind of electrode is less than 1 V. R-wave amplitude for sensing in this electrode should be more than 5 mV. An approximate 90 degree electrode loop is recommended inside the LV cavity (Figure 17). Purse-string sutures in the apex should be tied to restrict the movement of the electrode through the apex, and they should also be gently tied to the body of the electrode to stabilize position (Figure 15/C).

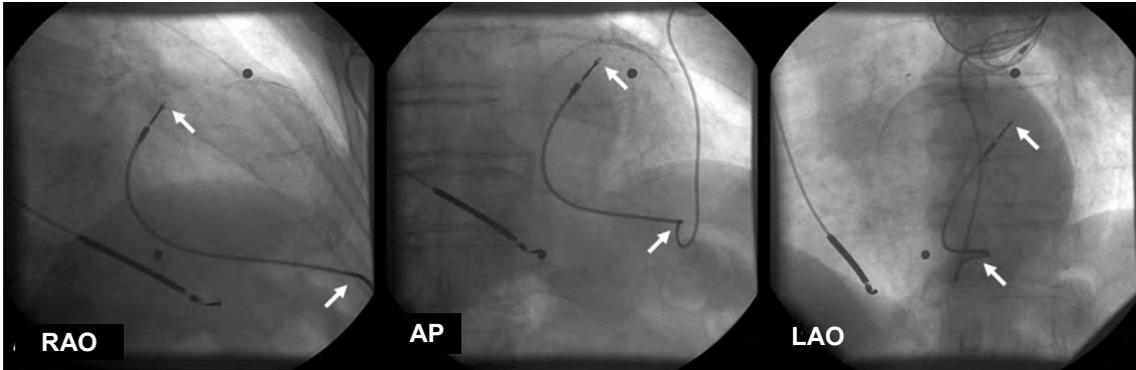


Figure 17

Chest X-ray after LV lead insertion and fixation

RAO= Right-Anterior-Oblique 30° view; AP= Antero-Posterior view;

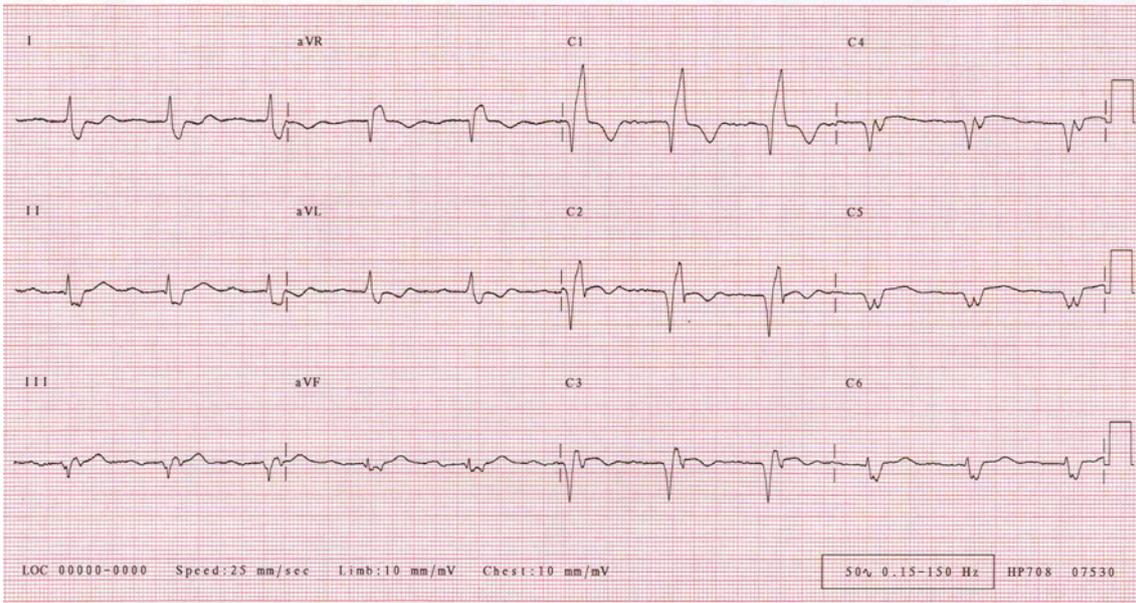
LAO= Left-Anterior-Oblique 45° view

The endocardial LV lead is indicated by white arrows at the apex and at the endocardial fixation with screw-in mechanism of the tip.

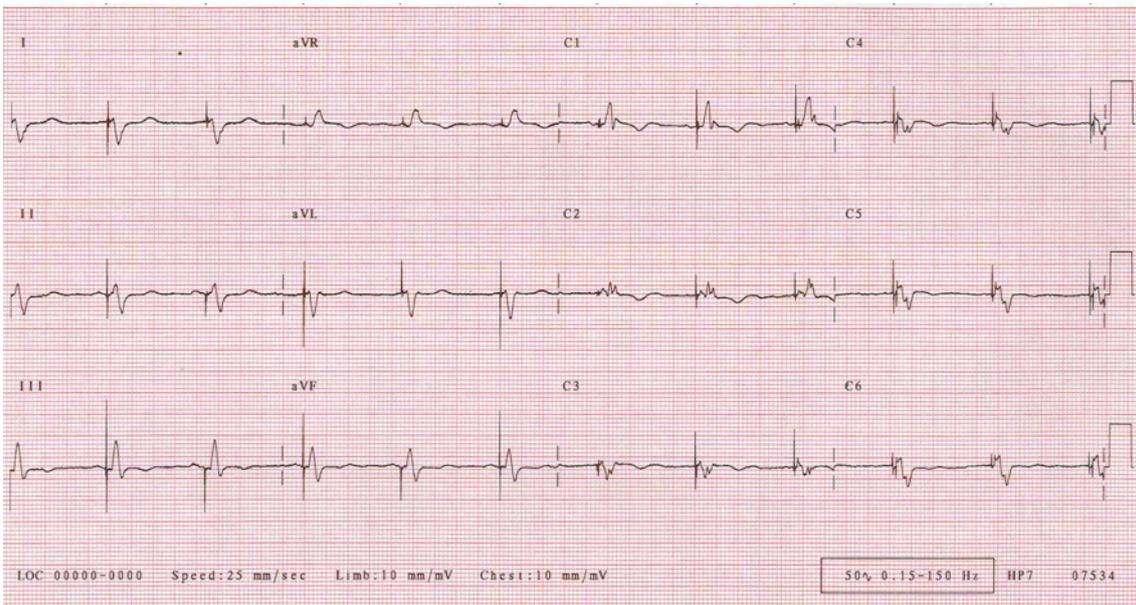
Before closing the chest wall, the lead should be subcutaneously tunneled through to the generator pocket. Before connecting to the generator, the lead connector should be cleaned to have all subcutaneous tissue removed.

Following LV electrode implantation the patient should be anticoagulated with a target anticoagulation level identical to mechanical valve prostheses.

After implantation the typical changes observed on ECG revealed that bi-ventricular pacing was effective (Figure 18).



A: ECG before implantation



B: ECG after implantation

Figure 18

We have planned a series of studies to evaluate our new method.

The aim of the first prospective, non-randomized study was to demonstrate the feasibility of this fundamentally new approach for endocardial LV lead implantation.

We performed twelve transapical LV lead implantations in ten end-stage heart failure patients (Table 3) as an alternative method after failed CS lead implantation (Table 4).

Table 3: Features of transapical LV lead implantations

Pt	Op	Age (yrs)	Gender	Transapical LV lead	Follow-up (months)	NYHA	
						pre	post
1.	1.	72	M	Guidant , 4096,52cm, 8Fr	13	IV	II
2.	2.	57	F	Vitatron , ICQ09B,52cm, 7Fr	10	IV	III
3.	3.	57	M	Vitatron , ICQ09B,52cm, 7Fr	10	IV	II
4.	4.	69	F	Medtronic , 4076,85cm, 7Fr	9	IV	II
5.	5.	53	M	Guidant , 4096,52cm, 8Fr	9	IV	III
6.	6.	65	M	Vitatron , ICQ09B,52cm, 7Fr	8	IV	
	7. due to lead dislocation		Medtronic , 4076,85cm, 7Fr			II	
7.	8.	53	M	Medtronic , 4076, 85cm, 7Fr	8	IV	II
8.	9.	46	M	Medtronic , 5076, 52cm, 7Fr	2	IV	
	10. due to pocket infection		Medtronic , 5076, 52cm, 7Fr			III	
9.	11.	71	M	Medtronic , 4076, 85cm, 7Fr	2	IV	II
10.	12.	57	M	Medtronic , 5076, 52cm, 7Fr	1	IV	II

Table 4

Classification of failed CS lead placements

Causes of CS lead placement failure	No.
Aberrant orifice of CS; no intubation	4
Phrenic nerve stimulation; high threshold	3
No suitable CS side branches	1
Recurrent dislocation of CS lead	2

All patients signed the written informed consent before the procedure.

In eight patients, there were no major and minor complications related to this new technique. During the follow up period (mean 7.2 ± 4.07 months), all patients responded favorably to the treatment. One lead dislocation and one pocket infection case was detected; lead repositioning and replacing could be performed without re-opening the pleural cavity. One patient's symptoms did not change, however, the numbers of hospitalizations decreased and the associated New York Heart Association functional class improved. Technically, all implanted and two replaced leads are working properly. One episode of self-terminating ventricular tachycardia has been detected by one of the implantable cardioverter defibrillators.

To achieve CRT, alternative methods are necessary for patients where CS lead implantation has failed. Epicardial pacing lead implantation is the most frequently used procedure, although this approach requires heart surgery. Due to LV dilatation, reaching the target area and pacing the most delayed segment of the lateral wall can be difficult, in some cases even impossible. Pericardial adhesions, which can be fairly common in this group of patients, can hide the location of the epicardial coronaries. Avoiding the damage of important vessels whilst inserting the epicardial lead is a great challenge. Furthermore, epicardial pacing seems to be less optimal than endocardial pacing. An activation sequence originating from the endocardial surface has advantages over epicardial stimulation. Endocardial stimulation has shown to be associated with a greater aortic and mitral time velocity integral, an increased left ventricular fractional

shortening and an improvement in the regional electromechanic delay in comparison with epicardial stimulation (27). There are studies showing endocardial leads which were implanted through the atrial septum and mitral valve that have also achieved similar results (27, 28). We strongly believe that additional risks are not negligible. When a foreign body enters the left side of the heart from the right atrium and is in close and permanent contact with the mitral valve, it increases the risk of mitral endocarditis (PUBL. 12). The transapical method we developed can overcome most of the above-mentioned potential problems. Furthermore, it provides an alternative for highly burdened patients. The advantages of this transapical technique are that it is minimally invasive, provides endocardial pacing and avoids problems caused by the contact with the mitral valve.

Comparing the transapical endocardial and epicardial resynchronization therapies

Our second study was entitled „Comparing the transapical endocardial and epicardial resynchronization therapies”, and the aim of this prospective, non-randomized study was to compare the two different operative strategies for LV pacing.

In 12 end-stage heart failure patients (mean age 62.9 ± 7.9 yrs, mean LVEF $26.1 \pm 7.1\%$, mean LVd 72.2 ± 8.5 mm), epicardial LV leads were implanted surgically using a limited left lateral thoracotomy. Ten end-stage heart failure patients (mean age 59.4 ± 7.9 yrs, mean LVEF $28.1 \pm 9.2\%$, mean LVd 70.6 ± 7.6 mm) underwent transapical LV lead implantation.

Over the 9-month follow up period, all patients in the transapical group responded favorably to the treatment (mean LVEF $33.5 \pm 4.3\%$, LVd 61.3 ± 6.1 mm). In the epicardial LV pacing group, similar results were obtained (mean LVEF $36.9 \pm 5.1\%$, LVd 65.1 ± 5.1 mm). Pacing parameters were assessed and we found a significant benefit related to transapically implanted LV leads.

The results reveal that LV transapical endocardial lead implantation is a feasible alternative in patients with failed CS approach when epicardial surgical lead placement is not an option. Some advantages of endocardial pacing have already been proved. Longer follow-up is warranted to evaluate the risk of thromboembolic complications.

Our plan for the near future: transapical pacing lead implantation into the systemic ventricle for CRT in congenital heart diseases, study protocol

CRT is very challenging in patients with congenital heart malformations or after cardiac surgery caused unavailable CS route (Figure 19), and in end stage heart failure.

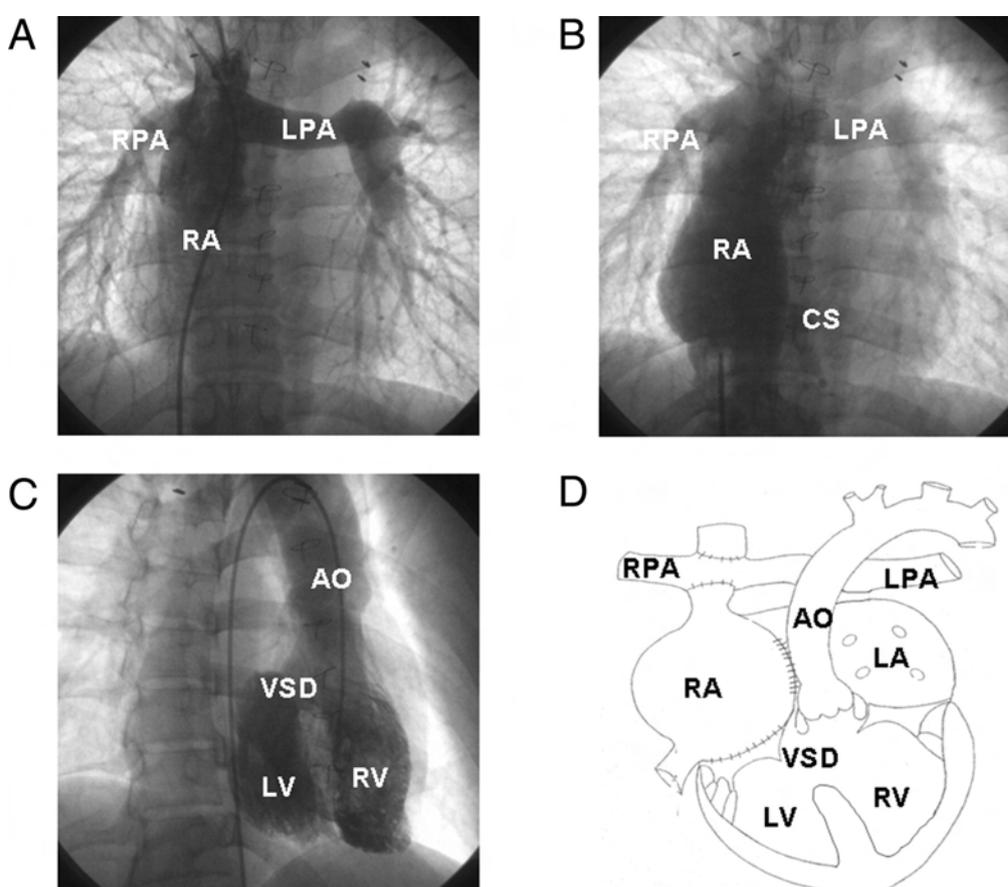


Figure 19

/A./B./C.: unavailable CS route proved by angiography

/D.: scheme of previous palliative surgery

To achieve the beneficial effects of transapical left ventricular lead implantation for these patients, we are planning an individual study in cooperation with colleagues in

Rotterdam. This study is planned to prove the safety and efficiency of a minimally invasive alternative method – the transapical route – to implant pacemaker leads into the systemic ventricle in order to achieve CRT in patients with impaired systemic ventricle long after surgery.

CS lead placement for transvenous LV pacing in CRT has a significant failure rate at implant and at short-term follow-up. Data was collected by studying a group of patients suffering from heart failure with certain forms of congenital heart malformations where the free wall of the systemic ventricle or any other walls could not be reached through the CS due to different reasons. For these patients, the failure rate of CS lead placement is almost 100%. The most frequent congenital malformations with the above mentioned consequences are univentricular hearts after Fontan operations and transpositions of the great arteries.

Before the development of our TA-CRT method, epicardial pacing lead or leads implantation was the only alternative. Epicardial pacing lead implantation can also be performed in a less invasive way by robotic surgery (30), however, this method has its own limitations too. Reaching the target area and pacing the most delayed segment of the lateral wall could be difficult and even impossible due to the intrathoracic location and anatomy of the dilated systemic ventricle. In this approach, pericardial adhesions, which are not rare in this group of patients, can hide the location of epicardial coronaries, so to protect these very important vessels from damages caused by the epicardial lead could also be difficult. We have found these pathologies in several cases and this was the main drive to perform TA-CRT in some patients.

Moreover, epicardial pacing seems to be less optimal than endocardial pacing, as described above. Additionally, there is some experience with endocardial lead implantation through the atrial septum passing the mitral valve. This kind of implantation might be performed in patients with transposition of the great arteries or with Fontan circulation through the AV valve after atrial septum or Fontan tunnel wall puncture, respectively. On the other hand we strongly believe that additional risks are not negligible using this technique. When a foreign body enters the systemic ventricle from the right atrium or from the Fontan tunnel having close and permanent contact

with the AV valve, it definitely increases the risk of infective endocarditis, involving the AV valve itself.

The TA-CRT technique for implantation of the systemic ventricular free-wall pacing lead or both ventricular pacing leads is less invasive than epicardial electrode placement, and the effectiveness of CRT is improved by the optimal pacing site, which is on one hand endocardial, and on the other hand freely chosen by additional endocardial mapping support. Device related infections result in less serious possible complications with the transapical route, because the lead enters the heart from the thoracic cavity, and does not have close contact with the AV valve apparatus inside the systemic ventricle.

TA-CRT can be performed through a minithoracotomy. A very small (3-4 cm) incision is enough to achieve safe apical access especially in this group of patients with severely enlarged ventricles. Reoperation is not a contraindication under these conditions.

Study aims

- Phase I) to prove feasibility of the TA-CRT method in this congenital patient group – 12 patients
- Phase II) comparing this technique to the epicardial lead implantation techniques – 20-20 patients

Study methods

Inclusion criteria

1. any patients with chronic heart failure in NYHA functional class III and IV in ambulatory conditions, with QRS duration ≥ 125 milliseconds and systemic ventricular ejection fraction $\leq 35\%$, **and** in whom percutaneous CS lead implantation has failed due to congenital malformation of the heart and/or previous cardiac operation to correct it
2. acceptance for surgical procedure by multidisciplinary team.

Exclusion criteria

1. Thrombus in the systemic ventricle cavity.
2. Acute or subacute myocardial infarction involving the apex.
3. Chest wall abnormalities near the apex.
4. Severe obstructive pulmonary disease.
5. Contraindication for anticoagulation.
6. Contraindication for narcosis.
7. Any (temporary) reason: fever, blood coagulation disorders, too high risk.

Additionally for *Phase II*): severe pericardial adhesions on the target area of epicardial electrodes.

Patients

For *Phase I*): 12 patients and a subgroup of 6 patients with endocardial mapping.

For *Phase II*): 20-20 patients in the TA-CRT and in the epicardial lead implantation groups based on randomization.

Randomization method for this study

Patients who are enrolled based on the inclusion and exclusion criteria and consented to participate are randomly assigned to undergo TA-CRT or epicardial lead implantation. Randomization is conducted using a computer and a sealed card system. The study coordinator notifies the surgeon of the study number and the surgeon opens the corresponding envelope. The surgeon and operating room staff are informed of the treatment assignment before starting the case.

Follow-up method for this study

Chest X-rays from antero-posterior and lateral-lateral projections, device interrogation/testing/programming and echocardiography (including evaluation of AV valve function) have to be performed before discharging the patients.

Ambulatory examinations to evaluate lead function and effectiveness of CRT have to be performed 1, 3, 6, and 12 months after the implantation.

Study data collection

The following data will be collected from each patient:

Age (at the operation), gender, body weight, body surface area, C/T index,

- Indication for CRT with etiology, cardio-pulmonary and other relevant co-morbidities (e.g. organic valve disease, indication for anticoagulation other than TA-CRT), previous cardiac and other intrathoracic operations,
- Echocardiographic data before CRT and at follow-up examinations: absolute and indexed ($/m^2$) dimensions of cardiac chambers and ventricular wall thickening, wall motion abnormalities other than asynchrony related, ejection fraction, tricuspid insufficiency and calculated pulmonary artery pressure,
- Data about asynchrony before CRT and at follow-up examinations: QRS duration, degree of asynchrony-related mitral insufficiency, tissue-Doppler imaging data about inter- and intraventricular delay,
- Report from the patients about the symptoms and functional capabilities before and after CRT, cardiac and other relevant medication before and after CRT,
- Results of the 6-minute hall-walk tests before CRT and at follow-up examinations,
- Data of implantation: date of operation, type of operation, length of skin incision, operation time, X-ray time, systemic ventricular lead type, sensing and threshold parameters, need for transfusion, duration of hospitalization,
- Reports of any method-related complications during the study period.

Study endpoints

For Phase I):

Primary: method-related morbidity during one-year follow-up.

Secondary:

- Wound healing without complications during follow-up.
- Acceptable electrical parameters during follow-up.
- Effectiveness of CRT during follow-up.

For Phase II):

Primary: Improvement in systemic ventricle ejection fraction status of patients in TA-CRT groups as compared to control groups during 6-month follow-up.

Secondary:

- Complications related to the systemic ventricle leads during follow-up.
- Number of hospital re-admissions.

Statistics

Standard statistical methods will be used to evaluate the collected data. Data will be collected in an MS-Excel file and evaluated with SPSS 13 software using a computer.

Based on this study protocol, we can evaluate all features of this new method in this patient group and can perform implantations with careful indications and patient selection.

5.

Conclusions

1. According to our results we would say that OPCAB is the most cost-effective method today for revascularization in two- and three-vessel CAD and in patients with one-vessel disease who are not suitable for PCI. The apical suction device improves the efficacy of OPCAB more than any other modification of this method.
2. Transapical cannula insertion through the left ventricle and the aortic valve into the proximal ascending aorta is the only life-saving arterial cannulation for emergency operations in acute proximal aortic dissection in a significant proportion of patients.
3. Safe application of long term mechanical circulatory support is indispensable for a successful pediatric heart transplantation program. We performed a modality of this treatment with success in Hungary too. One of the most important parts of the applied Berlin Heart[®] which can provide whole body perfusion is the left ventricular apical cannula.
4. CRT is the increasingly important treatment of heart failure. We performed the first transapical left ventricular endocardial lead implantation in the world. Our alternative method allows significantly more patients to be responders of CRT, because it is less invasive, safer and provides endocardial pacing.

6.

Summary

The apex is one of the most useful parts of the heart in surgical treatment although it does not often show pathological changes requiring surgical intervention. It has played an indispensable role in the appearance of the truly innovative surgical techniques and keeps it at present as well. These methods mean recovery and convalescence for millions of people with heart diseases. Some of the methods made the already existing techniques safer like the LV vent or the LV arterial cannula in dissections and last but not least the apical suction devices in OPCAB surgery. Some others have served as basis for new kinds of treatments which could have never appeared without the use of the cardiac apex. These are the alternative treatment options for aortic valve disease, the preferable implantation method in left ventricle assist device therapy, and the transapical lead implantation for completing CRT systems. The author of this thesis is well-trained and skilled in this field, only two of the above mentioned procedures are without his personal experience, one of them not being presented in Hungary at all. The OPCAB method without as well as – after its availability – with the apical suction device, and the arterial cannula through the LV apex for surgical treatment of acute proximal aortic dissection have been applied for the first time in Hungary by him, based on and proved by his detailed scientific research about surgery for coronary artery disease and aortic dissection. The first successful bridge-to-transplant long-term mechanical circulatory support in Hungary belongs to the team of the Gottsegen Hungarian Institute of Cardiology where he is in charge of this project. One of the most important parts of the applied Berlin Heart® BiVad system is the LV apical cannula. With close cooperation of his cardiologist colleagues, the author developed a fundamentally new approach for alternative LV lead implantation for CRT, and applied it with success first in the world. This method allows significantly more patients to be responders of this increasingly important treatment of heart failure. The scientific cardiac surgical works of the author detailed in this thesis prove the importance of the permanent requirement and implementation for innovative techniques in cardiac surgery despite the nowadays so frequent negative opinions about the general nightfall of this field of medicine.

Összefoglalás

A szívcsúcs számos vonatkozásban kiemelt jelentőségű a szívsebészeti tevékenység szempontjából, annak ellenére, hogy önmaga ritkán mutat beavatkozást indokoló patológiai elváltozást. A műtéti technikák forradalmi újításaiban a szívcsúcs szerepe a kezdetektől napjainkig nélkülözhetetlen. Szívbetegek milliói köszönhetik eredményes kezelésüket az így kialakított módszereknek. Az esetek egy részében már ismert eljárás vált biztonságosabbá: a szívcsúcsi dekompressziós balkamrai szívás, a szívcsúcsi artériás kanülálás akut aortadisszekcióban, és végül, de nem utolsó sorban az OPCAB műtéteknél a szívcsúcson tapadó pozicionáló eszköz sorolható ide. A szívcsúcs segítségével olyan módszerek is megjelenhettek, melyekre egyébként nem lett volna lehetőség, ezek a következők: az aortabillentyű betegségének alternatív kezelése, a tartós balkamrai keringéstámogató eszközök beültetése, és az alternatív balkamrai endokardialis ingerlés a reszinkronizációs kezelés részeként.

Jelen doktori tézisek szerzője kiemelkedő tapasztalatokkal rendelkezik ezen a területen, a felsorolt módszerek közül csak kettőt nem alkalmazott korábban, közülük az egyik még nincs a hazai gyakorlatban. A koszorúerek betegségének sebészi kezelése tekintetében folytatott tudományos kutatói, fejlesztői tevékenységének eredményeként OPCAB műtétet a szerző közölt elsőként Magyarországon (**Kassai I, et al. 1995.** Alternative method for coronary revascularization: surgery without cardiopulmonary bypass. *Card Hung.* 24(3): 14-6). Hasonló felkészülést követően elsőként alkalmazta a szívcsúcsi kanülálást akut proximális aortadisszekció műtéteihez. Az első sikeres „bridge-to-transplant” tartós mechanikus keringéstámogatás Magyarországon a Gottsegen György Országos Kardiológiai Intézetben történt, ahol a szerző ennek a programnak a megbízott koordinátora. Az alkalmazott Berlin Heart[®] mindkét szívfelet támogató műszív egyik legfontosabb része a balkamra csúcsi részéhez csatlakoztatott kanül. Szoros együttműködésben kardiológus kollégáival a szerző kifejlesztette és a világon elsőként, és sikerrel alkalmazta a reszinkronizációs kezeléshez alapvetően új alternatívaként a balkamrai elektróda endokardialis rögzítését a szívcsúcson keresztül történő bevezetéssel (**Kassai I, et al. 2008.** New method for cardiac resynchronization therapy: transapical endocardial lead implantation for left ventricular free wall pacing. *Europace.* 10(7): 882-3, és **Kassai I, et al. 2009.** Alternative method for cardiac

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A disszertációban a jelölt a szívsebészet területén végzett tudományos munkájával bizonyítja a folyamatos innováció és az így megjelenő új módszerek alkalmazásának jelentőségét, mely ékesen cáfolja a manapság gyakran felbukkanó véleményeket a szakterület hanyatlásáról.

7.

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9.

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